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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1 Web Page for STN Seminar Schedule - N. America  
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NEWS 3 APR 03 CAS coverage of exemplified prophetic substances  
enhanced  
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NEWS 7 APR 28 CAS patent authority coverage expanded  
NEWS 8 APR 28 ENCOMPLIT/ENCOMPLIT2 search fields enhanced  
NEWS 9 APR 28 Limits doubled for structure searching in CAS  
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NEWS 11 MAY 11 STN on the Web enhanced  
NEWS 12 MAY 11 BEILSTEIN substance information now available on  
STN Easy  
NEWS 13 MAY 14 DGENE, PCTGEN and USGENE enhanced with increased  
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introduction of free HIT display format  
NEWS 14 MAY 15 INPADOCDB and INPAFAMDB enhanced with Chinese legal  
status data  
NEWS 15 MAY 28 CAS databases on STN enhanced with NANO super role in  
records back to 1992  
NEWS 16 JUN 01 CAS REGISTRY Source of Registration (SR) searching  
enhanced on STN

NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,  
AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

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Enter NEWS followed by the item number or name to see news on that  
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\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 11:11:31 ON 18 JUN 2009

=> ile reg

ILE IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.22

0.22

FILE 'REGISTRY' ENTERED AT 11:11:46 ON 18 JUN 2009

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STRUCTURE FILE UPDATES: 16 JUN 2009 HIGHEST RN 1158716-03-0

DICTIONARY FILE UPDATES: 16 JUN 2009 HIGHEST RN 1158716-03-0

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TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

Please note that search-term pricing does apply when  
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REGISTRY includes numerically searchable data for experimental and  
predicted properties as well as tags indicating availability of  
experimental property data in the original document. For information  
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<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

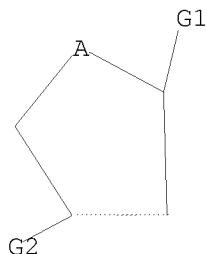
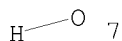
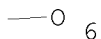
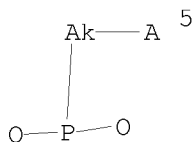
Uploading A:\10.598535.R1.Herdewijn et al..SRNT.CAPLUS.str

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



G1 [@1],[@2],[@3],[@4]

G2 [@5],[@6],[@7]

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss sam

SAMPLE SEARCH INITIATED 11:14:04 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 722089 TO ITERATE

0.3% PROCESSED 2000 ITERATIONS

6 ANSWERS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*INCOMPLETE\*\*

BATCH \*\*INCOMPLETE\*\*

PROJECTED ITERATIONS: 14394273 TO 14489287

PROJECTED ANSWERS: 40533 TO 46117

L2 6 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 11:14:12 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 14456437 TO ITERATE

4.3% PROCESSED 618174 ITERATIONS

1115 ANSWERS

8.7% PROCESSED 1256574 ITERATIONS

2638 ANSWERS

11.8% PROCESSED 1705093 ITERATIONS

4200 ANSWERS

13.6% PROCESSED 1961368 ITERATIONS

4288 ANSWERS

13.8% PROCESSED 2000000 ITERATIONS

4301 ANSWERS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.01.14

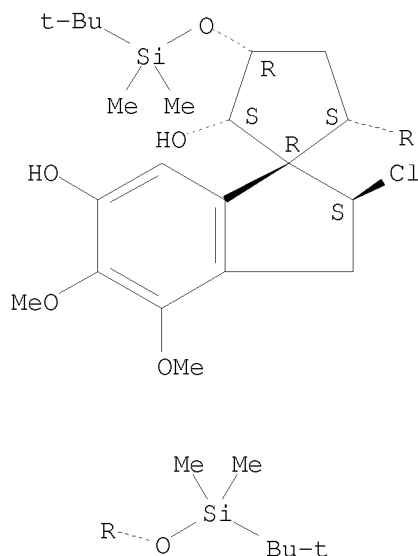
FULL FILE PROJECTIONS: ONLINE \*\*INCOMPLETE\*\*  
BATCH \*\*INCOMPLETE\*\*  
PROJECTED ITERATIONS: 14456437 TO 14456437  
PROJECTED ANSWERS: 30560 TO 31616

L3 4301 SEA SSS FUL L1

=> d scan

L3 4301 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN  
IN Spiro[cyclopentane-1,1'-[1H]indene]-2,6'-diol,  
2'-chloro-3,5-bis[[ (1,1-dimethylethyl)dimethylsilyl]oxy]-2',3'-dihydro-  
4',5'-dimethoxy-, (1R,2S,2'S,3R,5S)-  
MF C27 H47 Cl O6 Si2

Absolute stereochemistry. Rotation (+).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	189.24	189.46

FILE 'CAPLUS' ENTERED AT 11:16:22 ON 18 JUN 2009  
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FILE COVERS 1907 - 18 Jun 2009 VOL 150 ISS 25  
FILE LAST UPDATED: 17 Jun 2009 (20090617/ED)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2009  
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2009

Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his

(FILE 'HOME' ENTERED AT 11:11:31 ON 18 JUN 2009)

FILE 'REGISTRY' ENTERED AT 11:11:46 ON 18 JUN 2009

L1 STRUCTURE UPLOADED  
L2 6 S L1 SSS SAM  
L3 4301 S L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 11:16:22 ON 18 JUN 2009

=> s 13 and threos?

352 L3  
669 THREOS?  
L4 0 L3 AND THREOS?

=> s 13

L5 352 L3

=> s 15 and hiv

85291 HIV  
L6 11 L5 AND HIV

=> d 16 ed ibib abs hitstr 1-11

L6 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

ED Entered STN: 17 Apr 2009

ACCESSION NUMBER: 2009:457416 CAPLUS

DOCUMENT NUMBER: 150:423517

TITLE: Preparation of proline-containing peptides, especially spiropyrrolidine derivatives, and their use against HCV and HIV infection

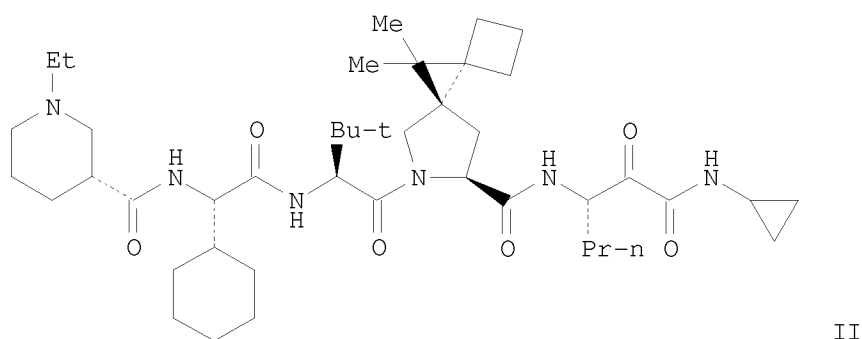
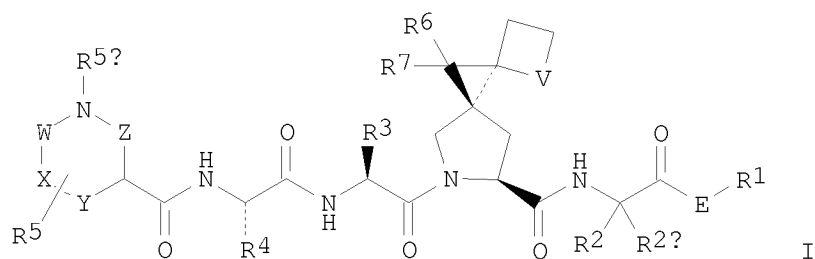
INVENTOR(S): Britt, Shawn D.; Ciszewski, Lech Andrzej; Fu, Jiping; Karur, Subramanian; Liu, Yugang; Parker, David Thomas; Prashad, Mahavir; Raman, Prakash; Seepersaud, Mohindra; Zheng, Rui; Lu, Peichao; Rigollier, Pascal; Yifru, Aregahegn

PATENT ASSIGNEE(S): Novartis AG, Switz.

SOURCE: PCT Int. Appl., 244pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009047264	A1	20090416	WO 2008-EP63460	20081008
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20090137495	A1	20090528	US 2008-249186	20081010
PRIORITY APPLN. INFO.:			US 2007-978974P	P 20071010
OTHER SOURCE(S):			MARPAT 150:423517	
GI				



AB Title compds. I [X = absent, NR5a, O; Y = (CH2)<sub>k</sub>; Z = (CH2)<sub>i</sub>; i, k = independently 0-4; W = (CH2)<sub>j</sub>; j = 1-4, wherein 2 ≤ i+j+k ≤ 5 when X is absent and 1 ≤ i+j+k ≤ 4 when X = O; V = (CH2)<sub>p</sub>; p = 0-3; E = OH, NH2, NH-alkyl, CONH, NHSO2; R1 = absent, H, alkyl, cycloalkyl; R2 = halo/cycloalkyl/alkyl; R2a = H, R2; R2 and R2a taken in combination form an (un)substituted 3-7 membered saturated ring comprising 0-1 N, O or S ring atoms; R3, R4 = independently alkyl,

cycloalkyl, cycloalkyl substituted with an alkyl; R5 = 0-3 residues each independently selected at each occurrence from H, halo, NH2, alkoxyalkyl, etc.; R5a = independently selected at each occurrence from H, haloalkyl, hydroxyalkyl, etc.; R6, R7 = independently H, alkyl; and their pharmaceutically acceptable salts and stereoisomers] were prepared as HCV NS3-4A serine protease inhibitors for treating, preventing and/or ameliorating HCV and HIV infections and HCV-related disorders. Thus, II, prepared by a multi-step synthesis from N-(tert-butoxycarbonyl)-L-tert-butylglycine, showed HCV NS3-4A inhibitory activity.

IT 1141825-73-1P

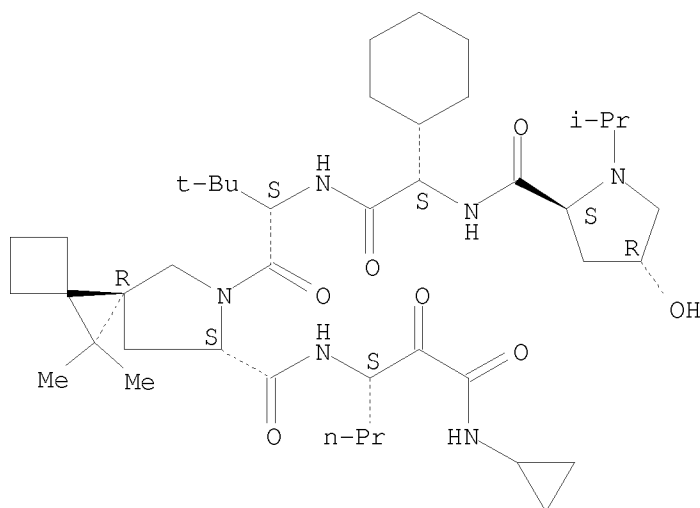
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of proline-containing peptides, especially spiropyrrolidine derivs., for treating HCV and HIV infections)

RN 1141825-73-1 CAPLUS

CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

ED Entered STN: 04 Mar 2009

ACCESSION NUMBER: 2009:257309 CAPLUS

DOCUMENT NUMBER: 150:463434

TITLE: SJ23B, a jatrophone diterpene activates classical PKCs and displays strong activity against HIV in vitro

AUTHOR(S): Bedoya, Luis M.; Marquez, Nieves; Martinez, Natalia; Gutierrez-Eisman, Silvia; Alvarez, Amparo; Calzado, Marco A.; Rojas, Jose M.; Appendino, Giovanni; Munoz, Eduardo; Alcami, Jose

CORPORATE SOURCE: Unidad de Inmunopatologia del SIDA, Centro Nacional de Microbiologia, Instituto de Salud Carlos III, Majadahonda, Madrid, 28220, Spain

SOURCE: Biochemical Pharmacology (2009), 77(6), 965-978  
CODEN: BCPA6; ISSN: 0006-2952

PUBLISHER: Elsevier B.V.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Existence of virus reservoirs makes the eradication of HIV infection extremely difficult. Current drug therapies neither eliminate these viral reservoirs nor prevent their formation. Consequently, new strategies are needed to target these reservoirs with the aim of decreasing their size. We analyzed a series of jatrophone diterpenes isolated from *Euphorbia hyberna* and we found that one of them, SJ23B, induces the internalization of the HIV-1 receptors CD4, CXCR4 and CCR5 and prevents R5 and X4 viral infection in human primary T cells at the nanomolar range. Moreover, SJ23B is a potent antagonist of HIV-1 latency. Using Jurkat-LAT-GFP cells, a model for HIV-1 latency, we found that prostratin and SJ23B activate HIV-1 gene expression, with SJ23B being at least 10-fold more potent than prostratin. SJ23B did not elicit transforming foci activity in NIH 3T3 cells but is a potent activator of PKC $\alpha$  and  $\delta$  as measured by in vitro kinase assays and by cellular translocation expts. By using isoform-specific PKC inhibitors we found that cPKCs are critical for SJ23B-induced HIV-1 reactivation. We also showed that both SJ23B-induced I $\kappa$ B $\alpha$  degradation and NF- $\kappa$ B activation were inhibited by the classical PKC inhibitor, Goe6976. Accordingly, SJ23B synergizes with ionomycin to translocate PKC $\alpha$  to the plasma membrane and to activate the NF- $\kappa$ B pathway. Moreover, SJ23B activates both NF- $\kappa$ B and Sp1-dependent transcriptional activities in primary T cells. We have shown that diterpene jatrophones represent a new member of anti-AIDS agents that could be developed for mitigating HIV reactivation.

IT 1147419-59-7 1147419-60-0 1147419-61-1  
1147419-62-2 1147419-63-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(jatrophone diterpene SJ23B activates classical PKCs and displays strong activity against HIV in vitro)

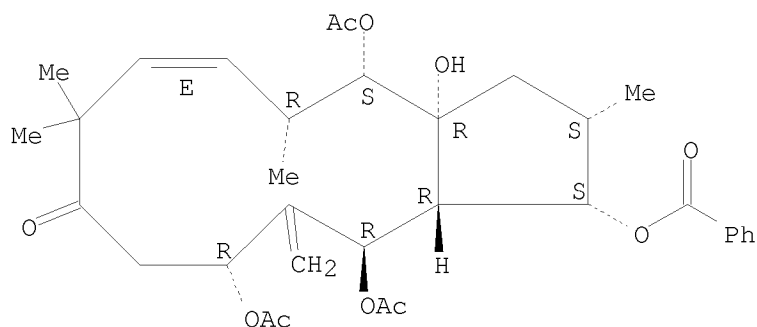
RN 1147419-59-7 CAPLUS

CN 8H-Cyclopentacyclododecen-8-one, 4,6,13-tris(acetyloxy)-3-(benzoyloxy)-1,2,3,3a,4,5,6,7,9,12,13,13a-dodecahydro-13a-hydroxy-2,9,9,12-tetramethyl-5-methylene-, (2R,3R,3aS,4S,6S,10E,12S,13R,13aS)-rel- (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as described by E or Z.

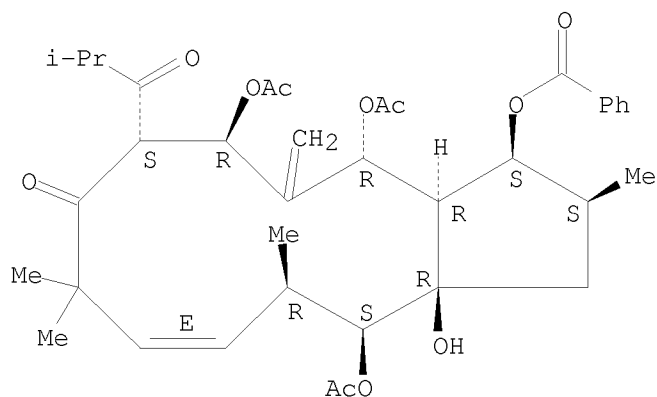
Currently available stereo shown.



RN 1147419-60-0 CAPLUS

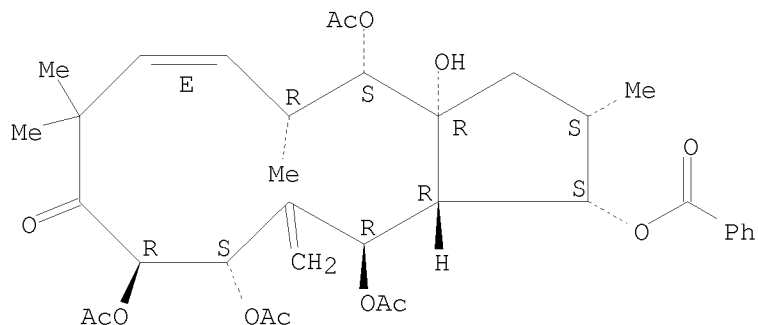
CN 8H-Cyclopentacyclododecen-8-one, 4,6,13-tris(acetyloxy)-3-(benzoyloxy)-1,2,3,3a,4,5,6,7,9,12,13,13a-dodecahydro-13a-hydroxy-2,9,9,12-tetramethyl-5-methylene-7-(2-methyl-1-oxopropyl)-, (2R,3R,3aS,4S,6S,7R,10E,12S,13R,13aS)-rel- (CA INDEX NAME)

Relative stereochemistry.  
Double bond geometry as described by E or Z.  
Currently available stereo shown.



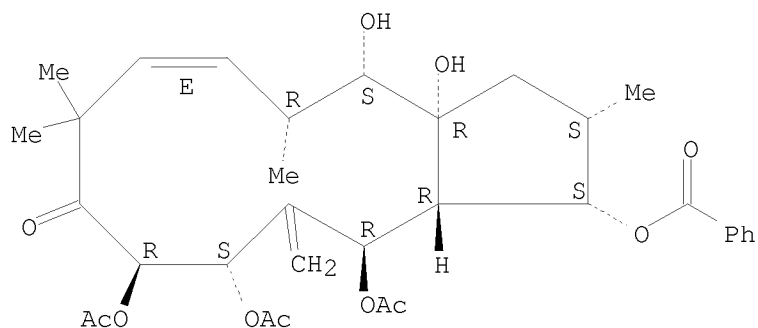
RN 1147419-61-1 CAPLUS  
CN 8H-Cyclopentacyclododecen-8-one, 4,6,7,13-tetrakis(acetyloxy)-3-(benzoyloxy)-1,2,3,3a,4,5,6,7,9,12,13,13a-dodecahydro-13a-hydroxy-2,9,9,12-tetramethyl-5-methylene-, (2R,3R,3aS,4S,6R,7S,10E,12S,13R,13aS)-rel- (CA INDEX NAME)

Relative stereochemistry.  
Double bond geometry as described by E or Z.  
Currently available stereo shown.



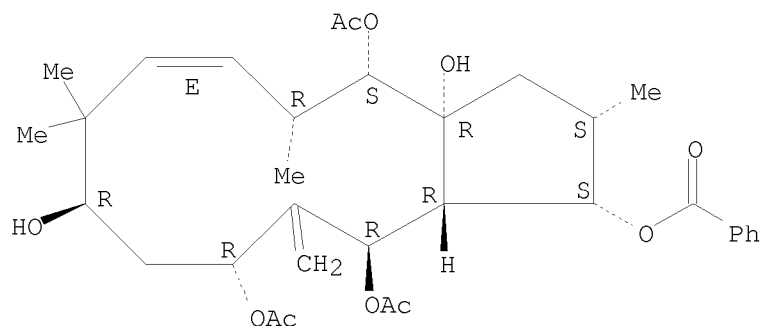
RN 1147419-62-2 CAPLUS  
CN 8H-Cyclopentacyclododecen-8-one, 4,6,7-tris(acetyloxy)-3-(benzoyloxy)-1,2,3,3a,4,5,6,7,9,12,13,13a-dodecahydro-13,13a-dihydroxy-2,9,9,12-tetramethyl-5-methylene-, (2R,3R,3aS,4S,6R,7S,10E,12S,13R,13aS)-rel- (CA INDEX NAME)

Relative stereochemistry.  
Double bond geometry as described by E or Z.  
Currently available stereo shown.



RN 1147419-63-3 CAPLUS  
 CN 3aH-Cyclopentacyclododecene-1,3a,4,9,11,13-hexol,  
 1,2,3,4,5,8,9,10,11,12,13,13a-dodecahydro-2,5,8,8-tetramethyl-12-methylene-  
 , 4,11,13-triacetate 1-benzoate, (1R,2R,3aS,4R,5S,6E,9S,11S,13S,13aS)-rel-  
 (CA INDEX NAME)

Relative stereochemistry.  
 Double bond geometry as described by E or Z.  
 Currently available stereo shown.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

ED Entered STN: 30 Jan 2009

ACCESSION NUMBER: 2009:116351 CAPLUS

DOCUMENT NUMBER: 150:191524

TITLE: Piperidine derivatives as chemokine receptor  
 modulators and their preparation, pharmaceutical  
 compositions and use in the treatment of diseases  
 INVENTOR(S): Gardner, Daniel S.; Duncia, John V.; Hynes, John;  
 Dhar, T. G. Murali; Carter, Percy H.; Santella, Joseph  
 B.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 167pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

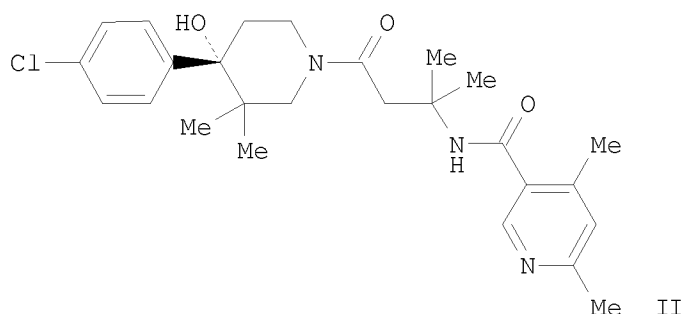
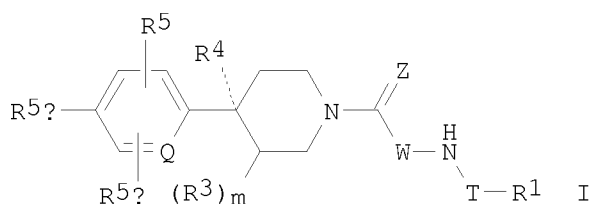
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009015164	A2	20090129	WO 2008-US70801	20080723
WO 2009015164	A3	20090423		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW  
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2007-951479P P 20070724  
 US 2008-81521P P 20080717  
 OTHER SOURCE(S): MARPAT 150:191524  
 GI



AB The invention describes piperidine derivs. of formula I and their stereoisomers, prodrugs and pharmaceutically acceptable salts, which are chemokine receptor modulators. In addition, methods of treating and preventing inflammatory diseases such as asthma and allergic diseases, as well as autoimmune pathologies such as rheumatoid arthritis and atherosclerosis using the modulators of formula I are disclosed. Compds. of formula I wherein Q is CH and N; Z is O and S; W is (un)substituted -CH<sub>2</sub>CH<sub>2</sub>-; T is CO, CO<sub>2</sub>, CONH and derivs., SO<sub>2</sub>, aminocyclobutenedione and derivs., and amino(cyanoimino)methyl and derivs.; R<sub>1</sub> is (un)substituted alkyl, (un)substituted cycloalkyl, (un)substituted (hetero)aryl and (un)substituted heterocyclyl; each R<sub>3</sub> is independently OH and alkyl; two of the R<sub>3</sub> may taken together with carbon atom attached to form 3- to 6-membered ring; R<sub>4</sub> is H, F, OH, CN and NH<sub>2</sub>; R<sub>5</sub> is H, halo, alkyl, CN and alkoxy; R<sub>5a</sub> is halo, CN and alkynyl; R<sub>5b</sub> is H, halo, CN, alkoxy and (un)substituted CO<sub>2</sub>CH<sub>2</sub>R<sub>10</sub>; R<sub>10</sub> is alkyl, alkenyl, alkynyl, (un)substituted aryl, (un)substituted arylalkyl, (un)substituted heterocyclyl and (un)substituted heterocyclylalkyl; m is 0-2; and their stereoisomers, prodrugs and pharmaceutically acceptable salts thereof, are claimed. Example compound II•TFA was prepared by a general procedure (procedure

given). All the invention compds. were evaluated for their chemokine receptor modulating activity. From the assay, it was determined that II•TFA exhibited an IC50 value of.

IT 1108153-48-5P 1108153-51-0P 1108154-06-8P

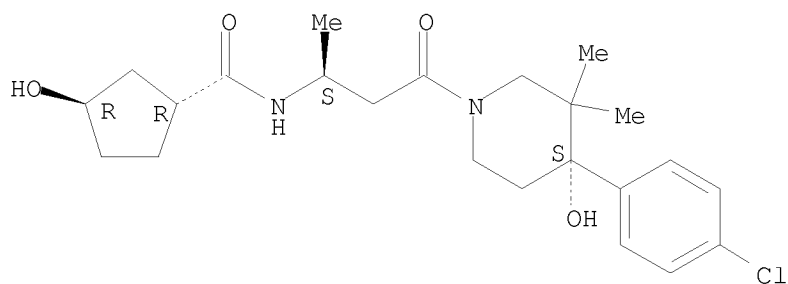
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of piperidine derivs. as chemokine receptor modulators useful in the treatment of diseases)

RN 1108153-48-5 CAPLUS

CN Cyclopentanecarboxamide, N-[(1S)-3-[(4S)-4-(4-chlorophenyl)-4-hydroxy-3,3-dimethyl-1-piperidiny]]-1-methyl-3-oxopropyl]-3-hydroxy-, (1R,3R)- (CA INDEX NAME)

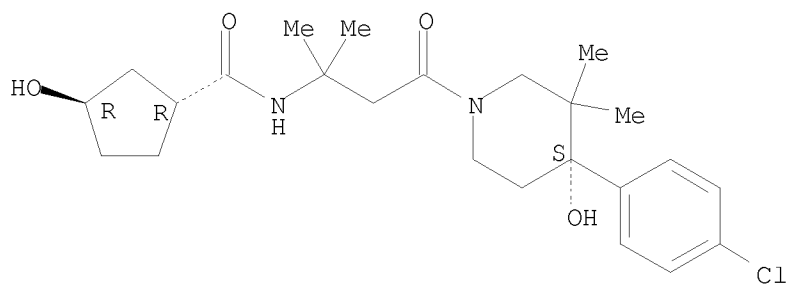
Absolute stereochemistry.



RN 1108153-51-0 CAPLUS

CN Cyclopentanecarboxamide, N-[3-[(4S)-4-(4-chlorophenyl)-4-hydroxy-3,3-dimethyl-1-piperidiny]]-1,1-dimethyl-3-oxopropyl]-3-hydroxy-, (1R,3R)- (CA INDEX NAME)

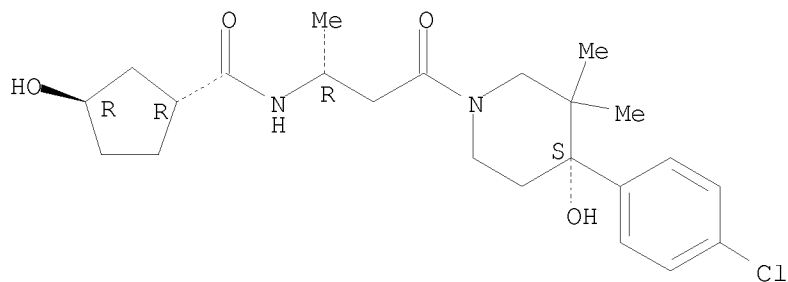
Absolute stereochemistry.



RN 1108154-06-8 CAPLUS

CN Cyclopentanecarboxamide, N-[(1R)-3-[(4S)-4-(4-chlorophenyl)-4-hydroxy-3,3-dimethyl-1-piperidiny]]-1-methyl-3-oxopropyl]-3-hydroxy-, (1R,3R)- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

ED Entered STN: 30 Jan 2009

ACCESSION NUMBER: 2009:115694 CAPLUS

DOCUMENT NUMBER: 150:168178

TITLE: Preparation of piperidine derivatives as modulators of chemokine receptor activity

INVENTOR(S): Santella, Joseph B.; Hynes, John; Gardner, Daniel S.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 185pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

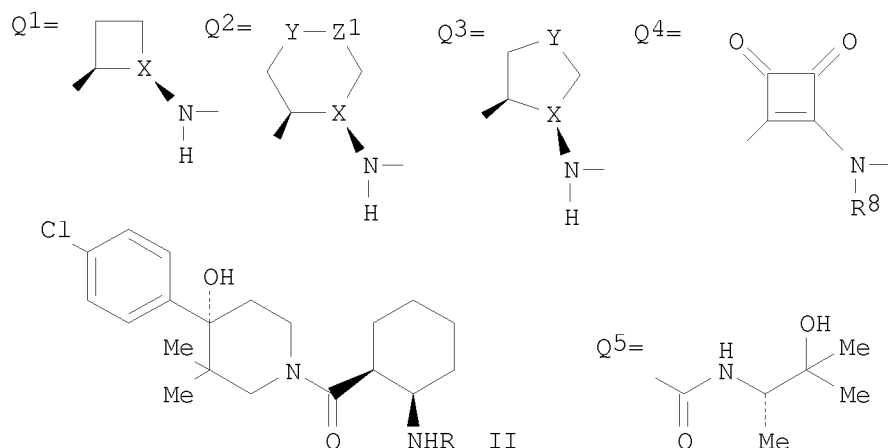
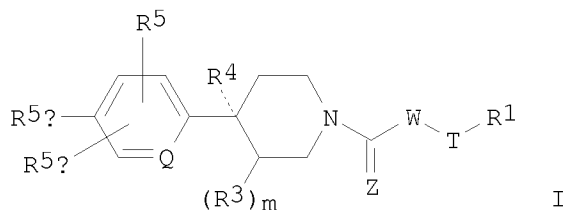
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009015166	A1	20090129	WO 2008-US70804	20080723
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2007-951478P P 20070724

US 2008-81529P P 20080717

OTHER SOURCE(S): MARPAT 150:168178

GI

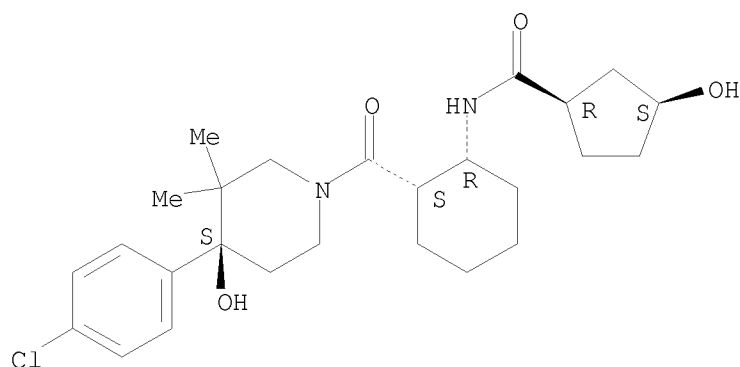


AB The present application describes modulators of MIP-1 of formula [I; Q = CH, N; Z = O, S; W = Q1, Q2, Q3; X = C(R8); Y = CH(R1a), CH2, O, S, S(O), S(O)2, N(R8), C(O), 1,3-dioxolan-2-ylidene; Z1 = CH(R7), CH2, O, S, N(R7), S(O), S(O)2; T = a bond, CO, C(O)O, CONR8, SO2, Q4, -C(:NCN)N(R8)-; R1 = each (un)substituted alkyl, cycloalkyl, aryl, heterocyclyl, or heteroaryl; R1a = alkyl, haloalkyl, aryl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocyclyl heterocyclylalkyl, halo, cyano, NO2, CO2H, etc.; R3 = OH, alkyl; or two R3's together with the carbon atom to which they are attached may form a 3- to 6-membered ring; R4 = H, F, OH, cyano, NH2; R5, R5b = H, halo, cyano, alkoxy; R5a = H, halo, cyano, alkynyl; R7 = alkyl, haloalkyl, aryl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocyclyl heterocyclylalkyl, halo, cyano, NO2, CO2H, etc.; R8 = H, alkyl; m = 0-2] or stereoisomers or pharmaceutically acceptable salts thereof. Methods of treating and preventing inflammatory diseases as well as autoimmune pathologies using the modulators are disclosed. In particular the above diseases include osteoarthritis, aneurysm, fever, cardiovascular effects, Crohn's disease, congestive heart failure, autoimmune diseases, HIV-infection, HIV-associated dementia, psoriasis, idiopathic pulmonary fibrosis, transplant arteriosclerosis, phys.- or chemical-induced brain trauma, inflammatory bowel disease, alveolitis, colitis, systemic lupus erythematosus, nephrotoxic serum nephritis, glomerularnephritis, asthma, multiple sclerosis, atherosclerosis, rheumatoid arthritis, restenosis, organ transplantation, and cancer. Thus, ((1S,2R)-2-aminocyclohexyl)[(S)-4-(4-chlorophenyl)-4-hydroxy-3,3-dimethylpiperidin-1-yl]methanone hydrochloride 25, benzoic acid 7.61, HOBt 19.08, EDC 23.88 mg and triethylamine (0.043 mL) were mixed in methylene chloride (3 mL) at 25° and stirred for 20 h to give, after workup, N-[(1R,2S)-2-[(4S)-4-(4-chlorophenyl)-4-hydroxy-3,3-dimethylpiperidine-1-carbonyl]cyclohexyl]benzamide (II; R = benzoyl) as a colorless oil. II (R = benzoyl) and compound II (R = Q5) reduced the specific binding of [125I]-MIP-1α to monocytic leukemia cells with IC50 of 2.1 and 0.7 μg/mL, resp.

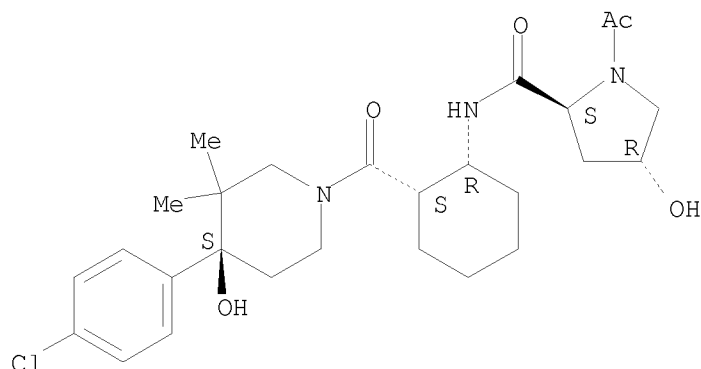
IT 1105702-73-5P 1105702-84-8P 1105702-89-3P

(preparation of piperidine derivs. as modulators of chemokine receptor activity for treating and preventing inflammatory diseases and autoimmune diseases)

CN Cyclopentanecarboxamide, N-[(1R,2S)-2-[[ (4S)-4-(4-chlorophenyl)-4-hydroxy-3,3-dimethyl-1-piperidinyl]carbonyl]cyclohexyl]-3-hydroxy-, (1R,3S)- (CA INDEX NAME)

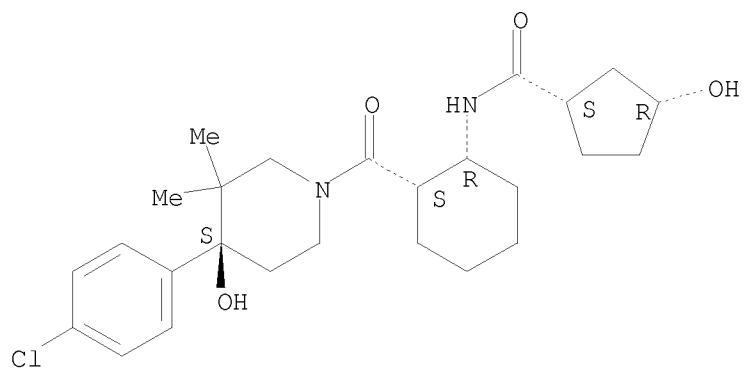


CN 2-Pyrrolidinecarboxamide, 1-acetyl-N-[(1R,2S)-2-[[[(4S)-4-(4-chlorophenyl)-4-hydroxy-3,3-dimethyl-1-piperidinyl]carbonyl]cyclohexyl]-4-hydroxy-, (2S,4R)- (CA INDEX NAME)



CN Cyclopentanecarboxamide, N-[(1R,2S)-2-[[ (4S)-4-(4-chlorophenyl)-4-hydroxy-3,3-dimethyl-1-piperidinyl]carbonyl]cyclohexyl]-3-hydroxy-, (1S,3R)- (CA INDEX NAME)

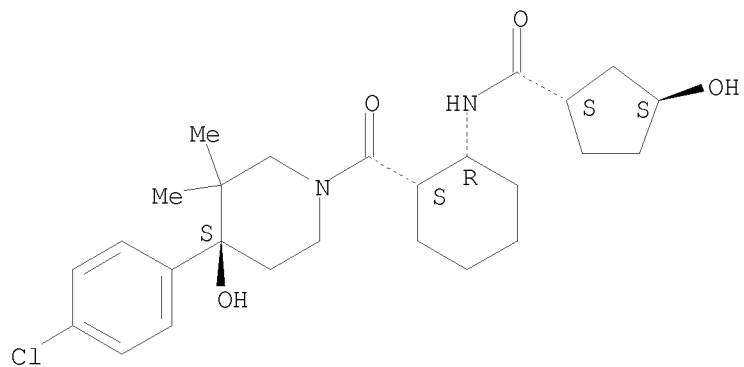
Absolute stereochemistry.



RN 1105702-90-6 CAPLUS

CN Cyclopentanecarboxamide, N-[(1R,2S)-2-[[[(4S)-4-(4-chlorophenyl)-4-hydroxy-3,3-dimethyl-1-piperidinyl]carbonyl]cyclohexyl]-3-hydroxy-, (1S,3S)- (CA INDEX NAME)

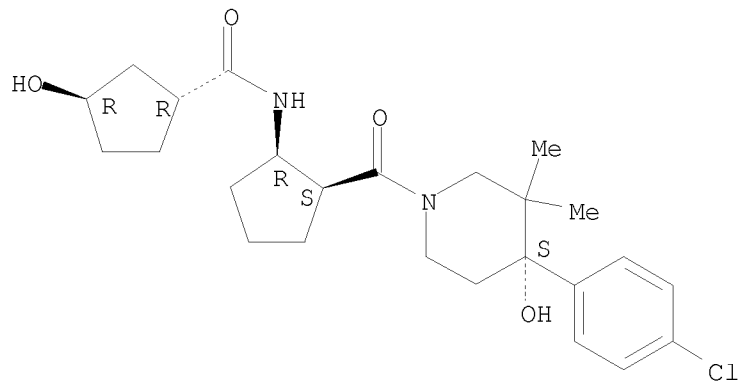
Absolute stereochemistry.



RN 1105702-99-5 CAPLUS

CN Cyclopentanecarboxamide, N-[(1R,2S)-2-[[[(4S)-4-(4-chlorophenyl)-4-hydroxy-3,3-dimethyl-1-piperidinyl]carbonyl]cyclopentyl]-3-hydroxy-, (1R,3R)- (CA INDEX NAME)

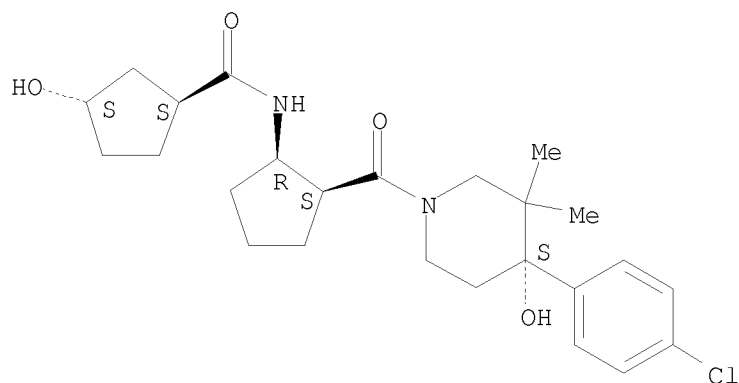
Absolute stereochemistry.



RN 1105703-00-1 CAPLUS

CN Cyclopentanecarboxamide, N-[(1R,2S)-2-[[ (4S)-4-(4-chlorophenyl)-4-hydroxy-3,3-dimethyl-1-piperidinyl]carbonyl]cyclopentyl]-3-hydroxy-, (1S,3S)- (CA INDEX NAME)

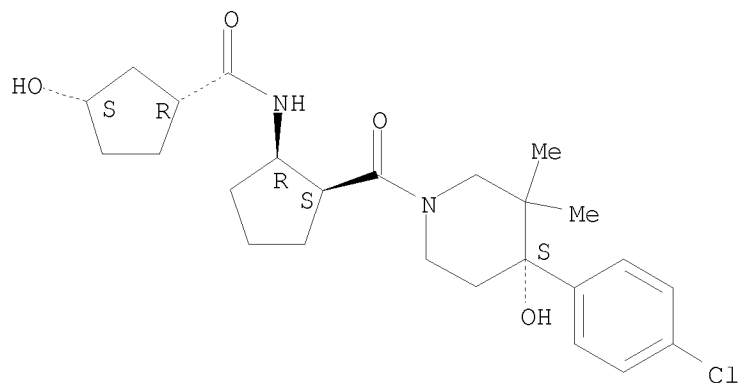
Absolute stereochemistry.



RN 1105703-01-2 CAPLUS

CN Cyclopentanecarboxamide, N-[(1R,2S)-2-[[ (4S)-4-(4-chlorophenyl)-4-hydroxy-3,3-dimethyl-1-piperidinyl]carbonyl]cyclopentyl]-3-hydroxy-, (1R,3S)- (CA INDEX NAME)

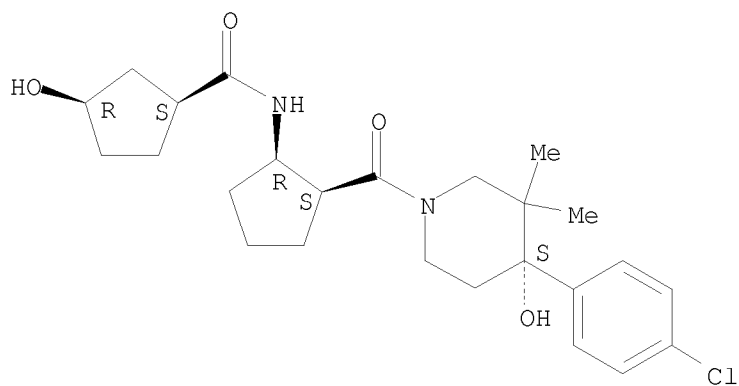
Absolute stereochemistry.



RN 1105703-02-3 CAPLUS

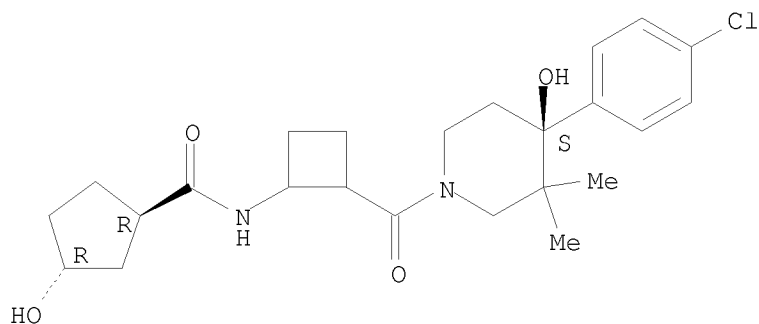
CN Cyclopentanecarboxamide, N-[(1R,2S)-2-[[ (4S)-4-(4-chlorophenyl)-4-hydroxy-3,3-dimethyl-1-piperidinyl]carbonyl]cyclopentyl]-3-hydroxy-, (1S,3R)- (CA INDEX NAME)

Absolute stereochemistry.



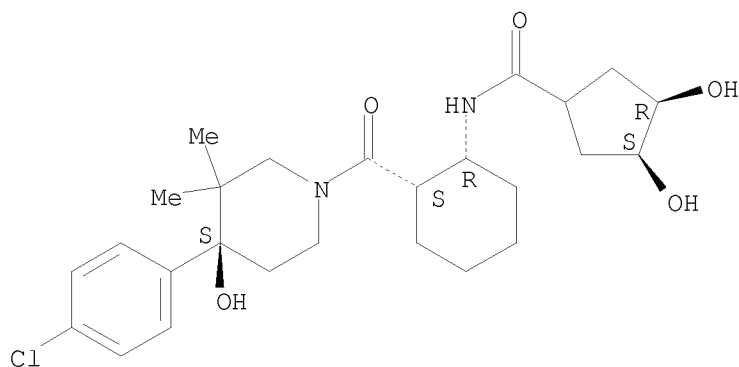
RN 1105703-17-0 CAPLUS  
 CN Cyclopentanecarboxamide, N-[2-[[ (4S)-4-(4-chlorophenyl)-4-hydroxy-3,3-dimethyl-1-piperidinyl]carbonyl]cyclobutyl]-3-hydroxy-, (1R,3R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 1106887-83-5 CAPLUS  
 CN Cyclopentanecarboxamide, N-[(1R,2S)-2-[[ (4S)-4-(4-chlorophenyl)-4-hydroxy-3,3-dimethyl-1-piperidinyl]carbonyl]cyclohexyl]-3,4-dihydroxy-, (3R,4S)- (CA INDEX NAME)

Absolute stereochemistry.

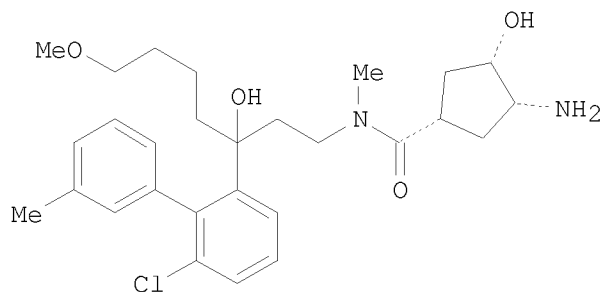
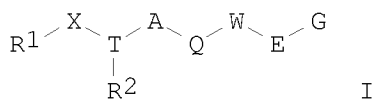


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ED Entered STN: 24 Dec 2008  
 ACCESSION NUMBER: 2008:1530131 CAPLUS  
 DOCUMENT NUMBER: 150:77252  
 TITLE: Preparation of aminobiphenylcyclopentanecarboxamide derivatives for use as renin inhibitors  
 INVENTOR(S): Baldwin, John J.; Cacatian, Salvacion; Claremon, David A.; Dillard, Lawrence W.; Flaherty, Patrick T.; Ishchenko, Alexey V.; Jia, Lanqi; McGeehan, Gerard; Simpson, Robert D.; Singh, Suresh B.; Tice, Colin M.; Xu, Zhenrong; Yuan, Jing; Zhao, Wei; Zhuang, Linghang; Zhang, Jing  
 PATENT ASSIGNEE(S): Vitae Pharmaceuticals, Inc., USA; SmithKline Beecham Corporation  
 SOURCE: PCT Int. Appl., 130pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008156831	A2	20081224	WO 2008-US7704	20080620
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2007-936380P P 20070620  
 OTHER SOURCE(S): MARPAT 150:77252  
 GI



II

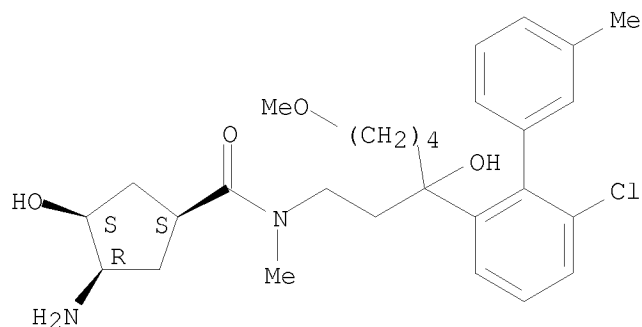
AB Title compds. I [A = CR<sub>4</sub>R<sub>5</sub>ZCR<sub>4</sub>R<sub>5</sub>; E = (un)substituted (un)saturated ring optionally bridged by (CH<sub>2</sub>)<sub>p</sub> composed of carbon and hetero atoms selected from N, O, or S; G = H, OH, (un)substituted alkyl, etc.; Q = C(O), C(S), S(O)<sub>2</sub>, etc.; T = N or CR<sub>3</sub>; W = bond or (un)substituted alkylene; X = (un)substituted Ph, benzo-1,3-dioxine, cycloalkyl, etc.; Z = O, S, CH<sub>2</sub>, etc.; R<sub>1</sub> = H, (un)substituted alkyl, aryl, etc.; R<sub>2</sub> = H, (un)substituted alkyl, alkenyl, etc.; R<sub>3</sub> = H, halo, alkyl, etc.; R<sub>4</sub> and R<sub>5</sub> independently = H, alkyl, or haloalkyl; or are taken together to form oxo; p = 1 to 3; with provisions], and their pharmaceutically acceptable salts, are prepared and disclosed as renin inhibitors. Thus, e.g., II was prepared by amidation of 3-(6-chloro-3'-methyl-2-biphenyl)-1-(methylamino)-7-methoxy-3-heptanol (preparation given) with (1S,3R,4S)-3-(((1,1-dimethylethyl)oxy)carbonyl)amino]-4-hydroxycyclopentanecarboxylic acid followed by deprotection. I were evaluated in renin inhibition assays, e.g., II demonstrated 50% inhibition at concns. of from approx. 50 nM to approx. 0.01 nM. I were disclosed as therapeutic agents that bind to renin or aspartic proteases to inhibit their activity.

IT 1093860-01-5P 1093860-03-7P 1093860-07-1P  
 1093860-09-3P 1093860-11-7P 1093860-12-8P  
 1093860-30-0P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of aminobiphenylcyclopentanecarboxamide derivs. for use as renin inhibitors)

RN 1093860-01-5 CAPLUS

CN Cyclopentanecarboxamide, 3-amino-N-[3-(6-chloro-3'-methyl[1,1'-biphenyl]-2-yl)-3-hydroxy-7-methoxyheptyl]-4-hydroxy-N-methyl-, (1S,3R,4S)- (CA INDEX NAME)

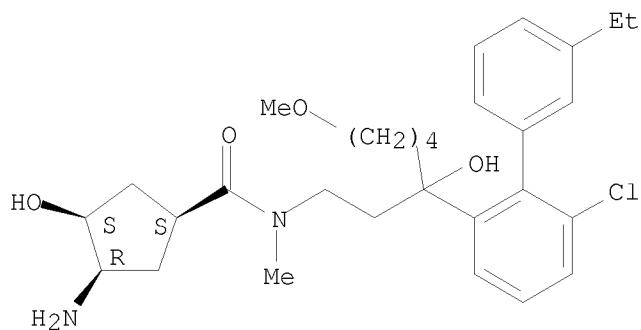
Absolute stereochemistry.



RN 1093860-03-7 CAPLUS

CN Cyclopentanecarboxamide, 3-amino-N-[3-(6-chloro-3'-ethyl[1,1'-biphenyl]-2-yl)-3-hydroxy-7-methoxyheptyl]-4-hydroxy-N-methyl-, (1S,3R,4S)- (CA INDEX NAME)

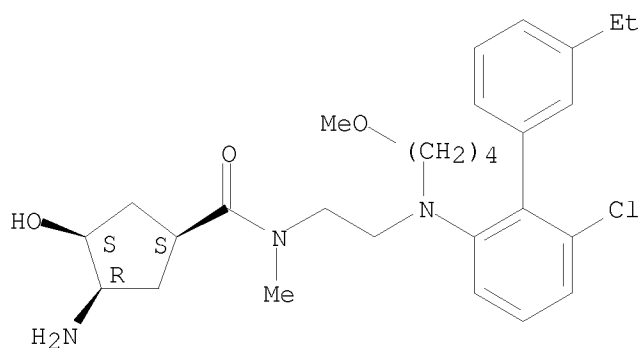
Absolute stereochemistry.



RN 1093860-07-1 CAPLUS

CN Cyclopentanecarboxamide, 3-amino-N-[2-[(6-chloro-3'-ethyl[1,1'-biphenyl]-2-yl)(4-methoxybutyl)amino]ethyl]-4-hydroxy-N-methyl-, (1S,3R,4S)- (CA INDEX NAME)

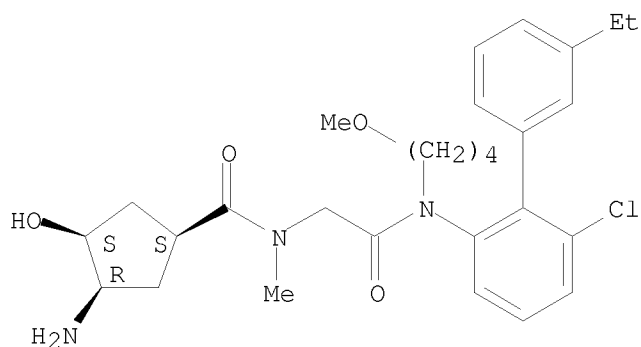
Absolute stereochemistry.



RN 1093860-09-3 CAPLUS

CN Cyclopentanecarboxamide, 3-amino-N-[2-[(6-chloro-3'-ethyl[1,1'-biphenyl]-2-yl)(4-methoxybutyl)amino]-2-oxoethyl]-4-hydroxy-N-methyl-, (1S,3R,4S)- (CA INDEX NAME)

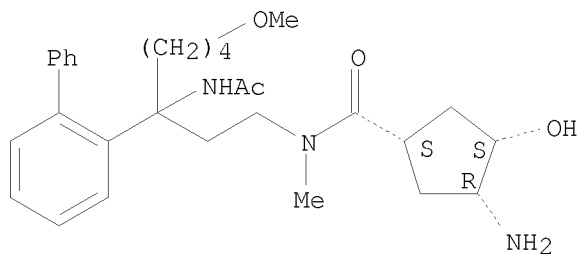
Absolute stereochemistry.



RN 1093860-11-7 CAPLUS

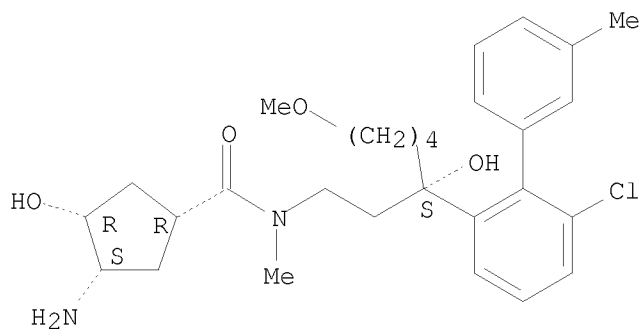
CN Cyclopentanecarboxamide, N-[3-(acetamido)-3-[1,1'-biphenyl]-2-yl]-7-methoxyheptyl]-3-amino-4-hydroxy-N-methyl-, (1S,3R,4S)- (CA INDEX NAME)

Absolute stereochemistry.



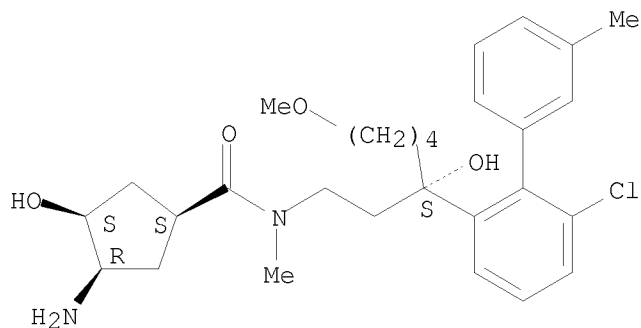
RN 1093860-12-8 CAPLUS  
 CN Cyclopentanecarboxamide, 3-amino-N-[(3S)-3-(6-chloro-3'-methyl[1,1'-biphenyl]-2-yl)-3-hydroxy-7-methoxyheptyl]-4-hydroxy-N-methyl-, (1R,3S,4R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 1093860-30-0 CAPLUS  
 CN Cyclopentanecarboxamide, 3-amino-N-[(3S)-3-(6-chloro-3'-methyl[1,1'-biphenyl]-2-yl)-3-hydroxy-7-methoxyheptyl]-4-hydroxy-N-methyl-, (1S,3R,4S)- (CA INDEX NAME)

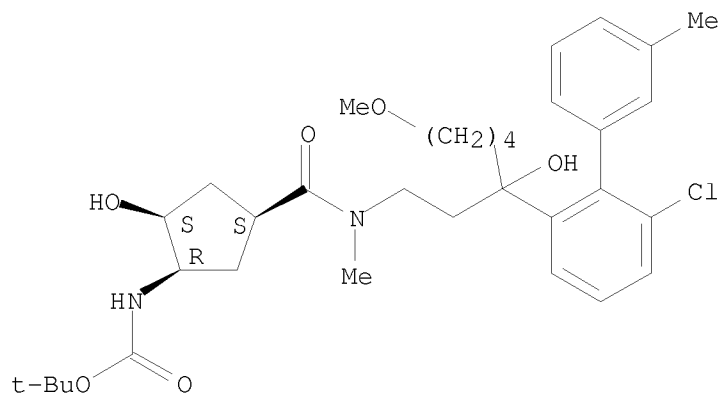
Absolute stereochemistry.



IT 1093860-26-4P 1093860-27-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of aminobiphenylcyclopentanecarboxamide derivs. for use as renin inhibitors)  
 RN 1093860-26-4 CAPLUS  
 CN Carbamic acid, N-[(1R,2S,4S)-4-[[[3-(6-chloro-3'-methyl[1,1'-biphenyl]-2-

yl)-3-hydroxy-7-methoxyheptyl]methylamino]carbonyl]-2-hydroxycyclopentyl]-  
, 1,1-dimethylethyl ester (CA INDEX NAME)

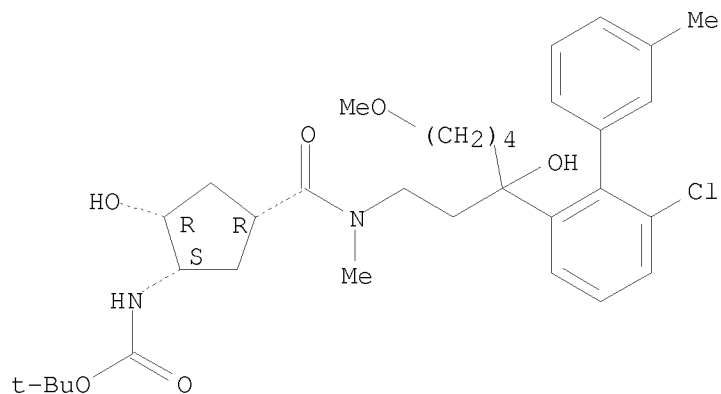
Absolute stereochemistry.



RN 1093860-27-5 CAPLUS

CN Carbamic acid, N-[(1S,2R,4R)-4-[[[3-(6-chloro-3'-methyl[1,1'-biphenyl]-2-yl)-3-hydroxy-7-methoxyheptyl]methylamino]carbonyl]-2-hydroxycyclopentyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

ED Entered STN: 09 Oct 2008

ACCESSION NUMBER: 2008:1217835 CAPLUS

DOCUMENT NUMBER: 150:15666

TITLE: Potent HIV-1 protease inhibitors  
incorporating meso-bicyclic urethanes as P2-ligands:  
structure-based design, synthesis, biological  
evaluation and protein-ligand X-ray studies

AUTHOR(S): Ghosh, Arun K.; Gemma, Sandra; Takayama, Jun;  
Baldrige, Abigail; Leshchenko-Yashchuk, Sofiya;  
Miller, Heather B.; Wang, Yuan-Fang; Kovalevsky,  
Andrey Y.; Koh, Yashiro; Weber, Irene T.; Mitsuya,  
Hiroaki

CORPORATE SOURCE: Departments of Chemistry and Medicinal Chemistry,  
Purdue University, West Lafayette, IN, 47907, USA

SOURCE: Organic & Biomolecular Chemistry (2008), 6(20),

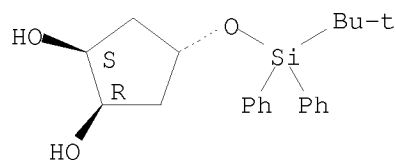
3703-3713  
 CODEN: OBCRAK; ISSN: 1477-0520  
 PUBLISHER: Royal Society of Chemistry  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 150:15666  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Recently, the authors designed a series of novel HIV-1 protease inhibitors incorporating a stereochem. defined bicyclic fused cyclopentyl (Cp-THF) urethane as the high affinity P2-ligand. Inhibitor I with this P2-ligand has shown very impressive potency against multidrug-resistant clin. isolates. Based upon the 1-bound HIV-1 protease x-ray structure, the authors have now designed and synthesized a number of meso-bicyclic ligands which can conceivably interact similarly to the Cp-THF ligand. The design of meso-ligands is quite attractive as they do not contain any stereocenters. Inhibitors incorporating urethanes of bicyclic-1,3-dioxolane and bicyclic-1,4-dioxane have shown potent enzyme inhibitory and antiviral activities. Inhibitor II ( $K_i = 0.11$  nM;  $IC_{50} = 3.8$  nM) displayed very potent antiviral activity in this series. While inhibitor III showed comparable enzyme inhibitory activity ( $K_i = 0.18$  nM) its antiviral activity ( $IC_{50} = 170$  nM) was significantly weaker than inhibitor 2. Inhibitor II maintained an antiviral potency against a series of multidrug resistant clin. isolates comparable to amprenavir. A protein-ligand x-ray structure of 3-bound HIV-1 protease revealed a number of key hydrogen bonding interactions at the S2-subsite. The authors have created an active model of inhibitor II based upon this x-ray structure.

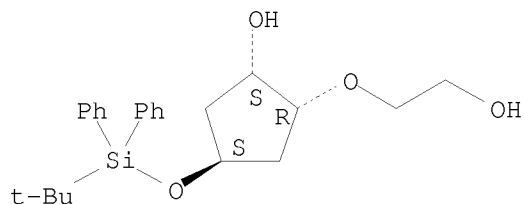
IT 1089180-27-7P 1089180-32-4P 1089180-41-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (structure-based design, synthesis, biol. evaluation and protein-ligand x-ray studies of potent HIV-1 protease inhibitors incorporating meso-bicyclic urethanes as P2-ligands)  
 RN 1089180-27-7 CAPLUS  
 CN 1,2-Cyclopentanediol, 4-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]-, (1R,2S)- (CA INDEX NAME)

Relative stereochemistry.



RN 1089180-32-4 CAPLUS  
 CN Cyclopentanol, 4-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]-2-(2-hydroxyethoxy)-, (1R,2S,4R)-rel- (CA INDEX NAME)

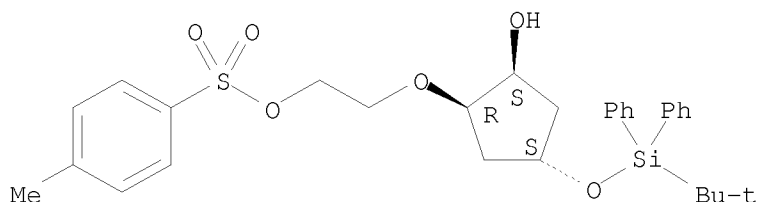
Relative stereochemistry.



RN 1089180-41-5 CAPLUS

CN Cyclopentanol, 4-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]-2-[2-[[[(4-methylphenyl)sulfonyl]oxy]ethoxy]-, (1R,2S,4S)-rel- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

ED Entered STN: 22 Sep 2008

ACCESSION NUMBER: 2008:1135389 CAPLUS

DOCUMENT NUMBER: 150:47298

TITLE: Design of hybrid inhibitors to HIV-1 protease

AUTHOR(S): Zhang, Da W.; Huang, Philip Lin; Lee-Huang, Sylvia; Zhang, John Z. H.

CORPORATE SOURCE: Department of Biochemistry, New York University School of Medicine, New York, NY, 10016, USA

SOURCE: Journal of Theoretical & Computational Chemistry (2008), 7(4), 485-503

CODEN: JTCCAC; ISSN: 0219-6336

PUBLISHER: World Scientific Publishing Co. Pte. Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

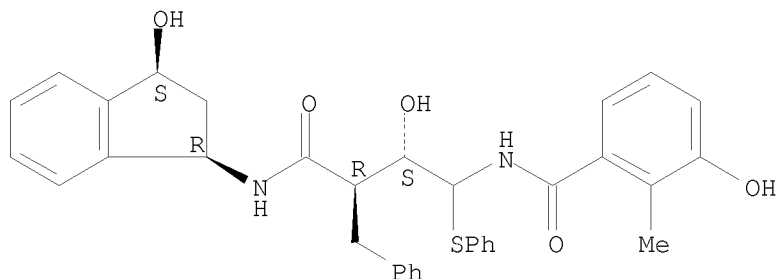
AB A series of HIV-1 protease (PR) inhibitors are designed to increase the binding affinity with PR subsites based on the quantum anal. of the contributions of mol. fragments in six FDA-approved PR drugs to the total binding interaction. The binding free energies were estimated by modified linear interaction energy approach [Zoete H, Michielin O, Karplus M, J Comput Aided Mol Des 17:861, 2003], in which the binding free energy is written as a linear combination of the electrostatic interaction energy between PR and the ligand, Eelec, the van der Waals interaction energy between PR and the ligand, EvdW, and the difference of the solvation free energies of the complex, the receptor and the isolated ligand,  $\Delta G_{solv}$ . The parameters of these energy terms were fitted for a training set of 14 HIV-1 protease-inhibitor complexes of known 3D structure with a correlation coefficient of 0.91 and an unsigned mean error of 0.83 kcal/mol.

IT 1093375-53-1

RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(design of hybrid inhibitors to HIV-1 protease based on

FDA-approved protease inhibitors and relation to binding interaction)  
RN 1093375-53-1 CAPLUS  
CN Benzenepropanamide, N-[(1R,3S)-2,3-dihydro-3-hydroxy-1H-inden-1-yl]-  
 $\alpha$ -[(1S)-1-hydroxy-2-[(3-hydroxy-2-methylbenzoyl)amino]-2-  
(phenylthio)ethyl]-, ( $\alpha$ R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

ED Entered STN: 04 Jul 2008

ACCESSION NUMBER: 2008:807536 CAPLUS

DOCUMENT NUMBER: 150:495075

TITLE: Synthesis and antiviral activity of 4'-modified carbocyclic nucleoside phosphonates (CNP)

AUTHOR(S): Mackman, R. L.; Boojamra, C. G.; Chen, J.; Feng, J.; Gao, Y.; Laflamme, G.; Lee, S.; Mabery, E.; Markevitch, D.; Parrish, J.; Perry, J.; Petrakovsky, O.; Ray, A. S.; Shih, I.-H.; Sperandio, D.; Vela, J.; Cihlar, T.

CORPORATE SOURCE: Gilead Sciences, Foster City, CA, 94404, USA

SOURCE: Collection Symposium Series (2008), 10 (Chemistry of Nucleic Acid Components), 191-195  
CODEN: CSYSFN

PUBLISHER: Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cyclopentenyl carbocyclic nucleoside phosphonates (CNP) containing a 4'-ethynyl, 4'-vinyl or 4'-Me group were designed to exploit new interactions in the active site of HIV reverse transcriptase (RT). The 4'-substituents were introduced stereoselectively onto a purine cyclopentenone intermediate using organometallic reagents transmetalated with cerium(III). The 4'-ethynyl analog demonstrated good antiviral activity in cell culture, and the diphosphate was found to be a potent inhibitor of HIV RT (IC<sub>50</sub> = 0.12  $\mu$ M). The synthesis was modified to afford 4'-ethynyl, 2',3'-dihydroxy cyclopentane analog, the diphosphate of which inhibited HCV NS5b polymerase in vitro.

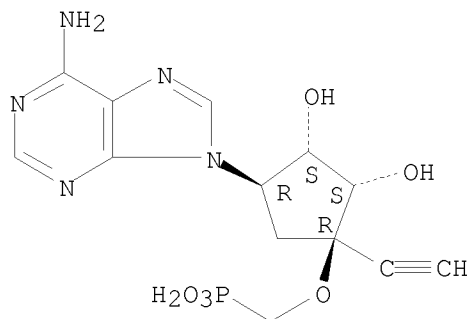
IT 1148035-71-5P 1148035-83-9P 1148035-84-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(synthesis and anti-HIV antiviral activity of 4'-modified cyclopentenyl carbocyclic nucleoside phosphonates)

RN 1148035-71-5 CAPLUS

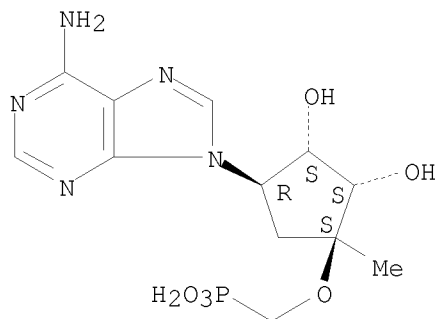
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



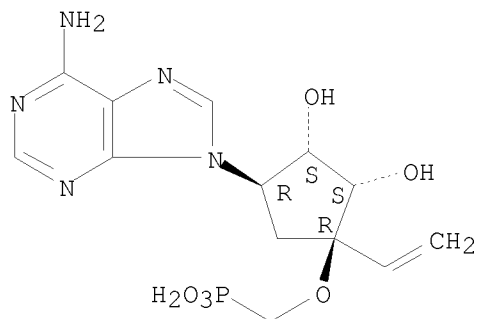
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CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



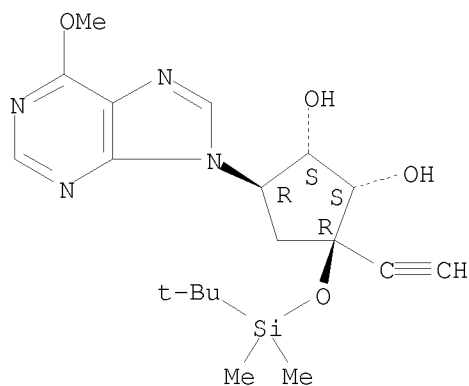
RN 1148035-84-0 CAPLUS  
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



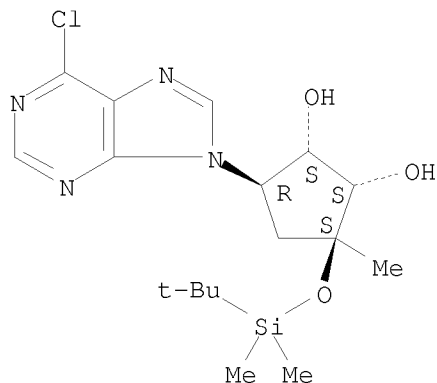
IT 1148035-66-8P 1148035-74-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(synthesis and anti-HIV antiviral activity of 4'-modified cyclopentyl carbocyclic nucleoside phosphonates)  
RN 1148035-66-8 CAPLUS  
CN 1,2-Cyclopentanediol, 3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-ethynyl-5-(6-methoxy-9H-purin-9-yl)-, (1S,2S,3R,5R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 1148035-74-8 CAPLUS  
 CN 1,2-Cyclopentanediol, 5-(6-chloro-9H-purin-9-yl)-3-[[ (1,1-dimethylethyl)dimethylsilyl]oxy]-3-methyl-, (1S,2S,3S,5R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

ED Entered STN: 14 May 2008

ACCESSION NUMBER: 2008:581440 CAPLUS

DOCUMENT NUMBER: 150:228

TITLE: Binding mode analyses and pharmacophore model development for sulfonamide chalcone derivatives, a new class of  $\alpha$ -glucosidase inhibitors

AUTHOR(S): Bharatham, Kavitha; Bharatham, Nagakumar; Park, Ki Hun; Lee, Keun Woo

CORPORATE SOURCE: Division of Applied Life Science (BK21 Program), Environmental Biotechnology National Core Research Center, Gyeongsang National University, Jinju, 660-701, S. Korea

SOURCE: Journal of Molecular Graphics & Modelling (2008), 26(8), 1202-1212

CODEN: JMGMEI; ISSN: 1093-3263

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

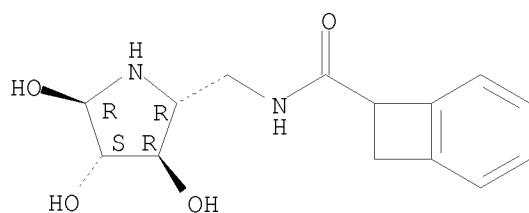
LANGUAGE: English

AB Sulfonamide chalcone derivs. are a new class of non-saccharide compds. that effectively inhibit glucosidases which are the major targets in the

treatment of type 2 diabetes and HIV infection. Our aim is to explore their binding mode of interaction at the active site by comparing with the sugar derivs. and to develop a pharmacophore model which would represent the critical features responsible for  $\alpha$ -glucosidase inhibitory activity. The homol. modeled structure of *Saccharomyces cerevisiae*  $\alpha$ -glucosidase was built and used for mol. docking of non-sugar/sugar derivs. The validated docking results projected the crucial role of NH group in the binding of sugar/non-sugar derivs. to the active site. Ligplot analyses revealed that Tyr71, and Phe177 form hydrophobic interactions with sugar/non-sugar derivs. by holding the terminal glycosidic ring mimics. Mol. dynamic (MD) simulation studies were performed for protein alone and with chalcone derivative to prove its binding mechanism as shown by docking/Ligplot results. It would also help to substantiate the homol. modeled structure stability. With the knowledge of the crucial interactions between ligand and protein from docking and MD simulation studies, features for pharmacophore model development were chosen. The CATALYST/HipHop was used to generate a five featured pharmacophore model with a training set of five non-sugar derivs. As validation, all the crucial features of the model were perfectly mapped onto the 3D structures of the sugar derivs. as well as the newly tested non-sugar derivs. Thus, it can be useful in virtual screening for finding new non-sugar derivs. as  $\alpha$ -glucosidase inhibitors.

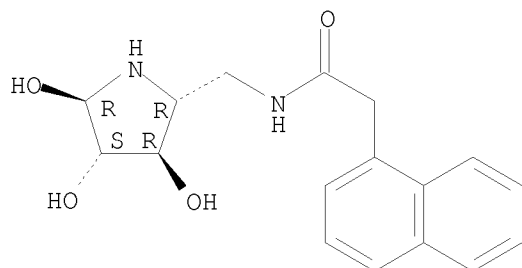
IT 1086378-38-2 1086378-42-8 1086378-46-2  
 RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action);  
 PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)  
 (binding mode analyses and pharmacophore model development for  
 sulfonamide chalcone derivs., a new class of  $\alpha$ -glucosidase  
 inhibitors)  
 RN 1086378-38-2 CAPLUS  
 CN Bicyclo[4.2.0]octa-1,3,5-triene-7-carboxamide,  
 N-[[ (2R,3R,4S,5R)-3,4,5-trihydroxy-2-pyrrolidinyl]methyl]- (CA INDEX  
 NAME)

Absolute stereochemistry.



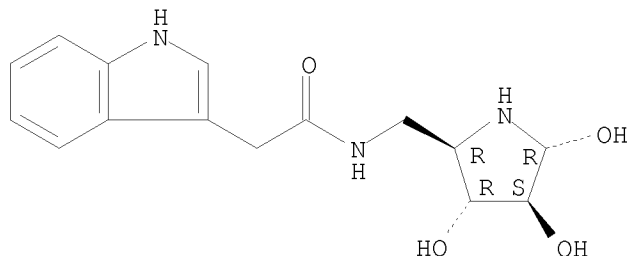
RN 1086378-42-8 CAPLUS  
 CN 1-Naphthaleneacetamide, N-[[ (2R,3R,4S,5R)-3,4,5-trihydroxy-2-  
 pyrrolidinyl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 1086378-46-2 CAPLUS  
CN 1H-Indole-3-acetamide, N-[[ (2R,3R,4S,5R)-3,4,5-trihydroxy-2-pyrrolidiny]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

ED Entered STN: 12 Nov 2004

ACCESSION NUMBER: 2004:965113 CAPLUS

DOCUMENT NUMBER: 141:411085

TITLE: Preparation of phosphonate prodrugs of antiviral compounds

INVENTOR(S): Boojamara, Constantine G.; Cannizzaro, Carina E.; Chen, James M.; Chen, Xiaowu; Cho, Aesop; Chong, Lee S.; Fardis, Maria; Jin, Haolun; Hirschmann, Ralph F.; Huang, Alan X.; Kim, Choung U.; Kirschberg, Thorsten A.; Lee, Christopher P.; Lee, William A.; Mackman, Richard L.; Markevitch, David Y.; Oare, David; Prasad, Vidya K.; Pyun, Hyung-Jung; Ray, Adrian S.; Sherlock, Rosemarie; Swaminathan, Sundaramoorthi; Watkins, Will; Zhang, Jennifer R.

PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA

SOURCE: PCT Int. Appl., 856 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 18

PATENT INFORMATION:

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PRIORITY APPLN. INFO.:

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US 2003-495630P	P	20030815
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US 2003-495632P	P	20030815
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US	2003-495760P	P	20030815
US	2003-495763P	P	20030815
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US	2003-510245P	P	20031010
US	2003-513531P	P	20031024
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US	2003-513979P	P	20031024
US	2003-513982P	P	20031024
US	2003-514021P	P	20031024
US	2003-514044P	P	20031024
US	2003-514051P	P	20031024
US	2003-514054P	P	20031024
US	2003-514075P	P	20031024

OTHER SOURCE(S):            MARPAT 141:411085

AB    The invention is related to phosphorus-substituted compds. (e.g. [[4-(4-hydroxy-6-methoxy-7-methyl-3-oxo-1,3-dihydroisobenzofuran-5-yl)-2-methylbut-2-enyl]oxy]methyl]phosphonic acid (1)) with antiviral activity (no data; e.g. hepatitis C), compns. containing such compds., and therapeutic methods that include the administration of such compds., as well as to processes and intermediates useful for preparing such compds. Many example prepns. are included. For example, 1 (83 %) and the corresponding mono-iso-Pr ester (7 %) were prepared by condensation of 7-hydroxy-6-((E)-4-hydroxy-3-methylbut-2-enyl)-5-methoxy-4-methyl-3H-isobenzofuran-1-one with diisopropyl bromomethylphosphonate in DMF in the presence of LiOtBu followed by deesterification using TMSBr and 2,6-lutidine in MeCN.

IT    1089678-21-6 1089678-28-3

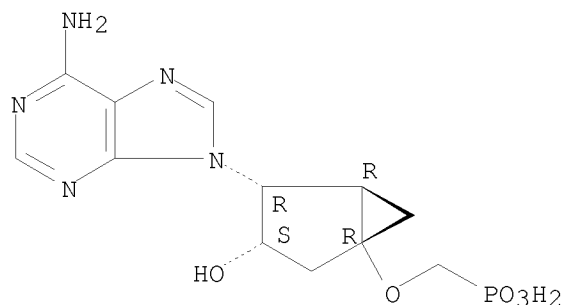
RL: PRPH (Prophetic)

(Preparation of phosphonate prodrugs of antiviral compounds)

RN    1089678-21-6    CAPLUS

CN INDEX NAME NOT YET ASSIGNED

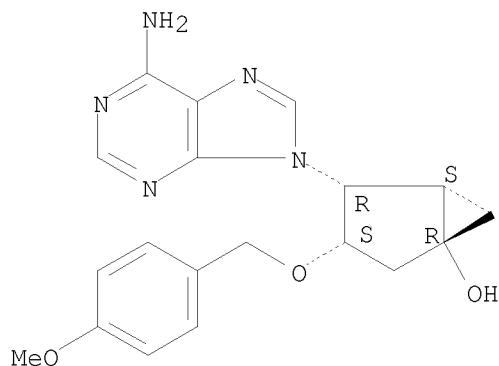
Absolute stereochemistry.



RN 1089678-28-3 CAPLUS

CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



L6 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2009 ACS on STN

ED Entered STN: 11 Jan 2001

ACCESSION NUMBER: 2001:25780 CAPLUS

DOCUMENT NUMBER: 134:86548

TITLE: Preparation of heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors

INVENTOR(S): Getman, Daniel P.; De Crescenzo, Gary A.; Freskos, John N.; Vazquez, Michael L.; Sikorski, James A.; Deyadas, Balekudru; Nagarajan, Srinivasan; Brown, David L.; McDonald, Joseph J.

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: U.S., 85 pp., Cont.-in-part of U. S. Ser. No. 402,419, abandoned

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6172101	B1	20010109	US 1998-894984	19980423

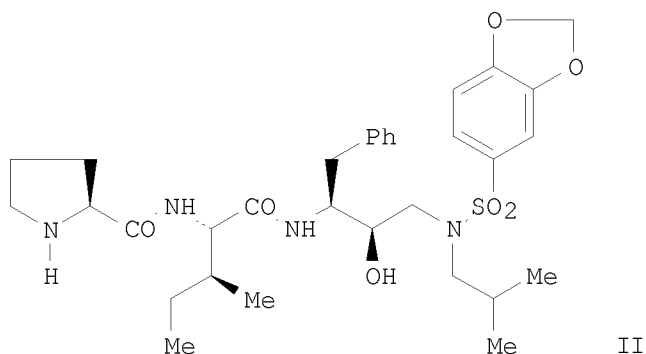
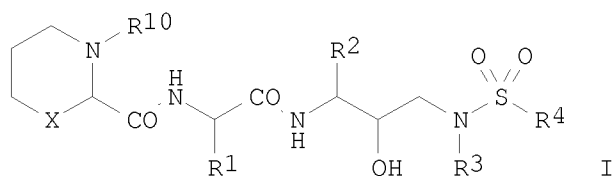
WO 9628465 A1 19960919 WO 1996-US2683 19960307  
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,  
ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT,  
LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,  
SG, SI

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,  
IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA

PRIORITY APPLN. INFO.:

US 1995-402419 B2 19950310  
WO 1996-US2683 W 19960307  
US 1995-474117 A2 19950607

OTHER SOURCE(S): MARPAT 134:86548  
GI



AB Heterocyclylcarbonyl amino acids, such as I [R1 = alkyl, alkenyl, alkynyl, etc.; R2 = alkyl, arylalkyl, alkylthioalkyl, arylthioalkyl, etc.; R3 = alkyl, cycloalkyl; R4 = aryl, heteroaryl; R10 = H, alkyl, nitrogen protecting group, etc., X = CH2, bond], were prepared for pharmaceutical use as HIV protease inhibitors for inhibiting retroviral proteases, such as human immunodeficiency virus (HIV) protease, prophylactically preventing retroviral infection or the spread of a retrovirus, and treatment of a retroviral infection. Thus, II was prepared by a multistep synthetic sequence starting from N-protected-L-phenylalanine, -L-isoleucine, -L-proline, isobutylamine, and 1,3-benzodioxole. The prepared heterocyclylcarbonyl amino acids were tested via an HIV inhibition assay.

IT 1140057-45-9 1140057-49-3 1140057-53-9  
1140057-56-2 1140057-60-8 1140057-64-2  
1140057-68-6 1140058-14-5 1140058-18-9  
1140058-22-5 1140058-26-9 1140058-29-2  
1140058-33-8 1140058-37-2 1140058-41-8  
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1140058-56-5 1140058-60-1

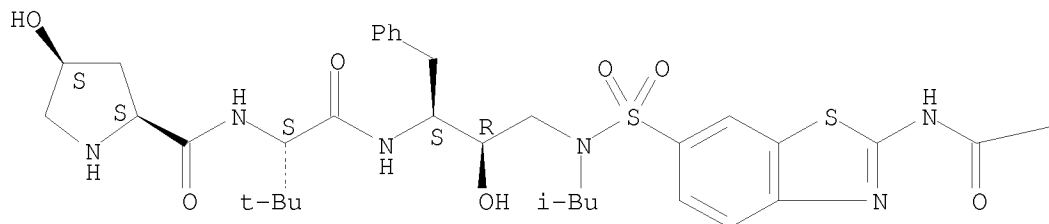
RL: PRPH (Prophetic)

(Preparation of heterocyclylcarbonyl amino acid hydroxyethylamino sulfonamide retroviral protease inhibitors)

RN 1140057-45-9 CAPLUS  
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

PAGE 1-A



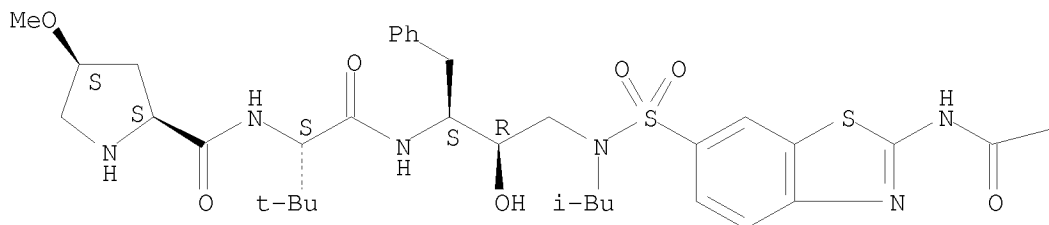
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RN 1140057-49-3 CAPLUS  
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

PAGE 1-A



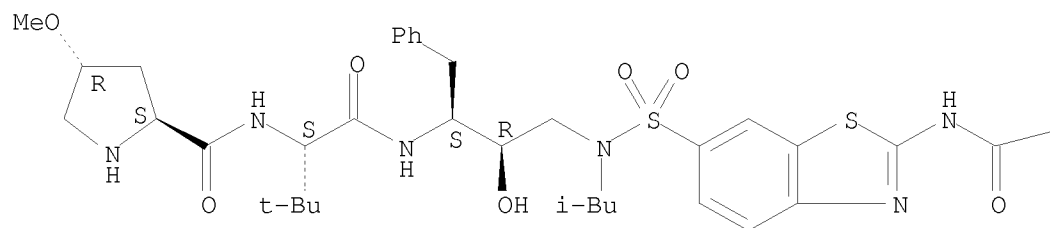
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Absolute stereochemistry.

PAGE 1-A

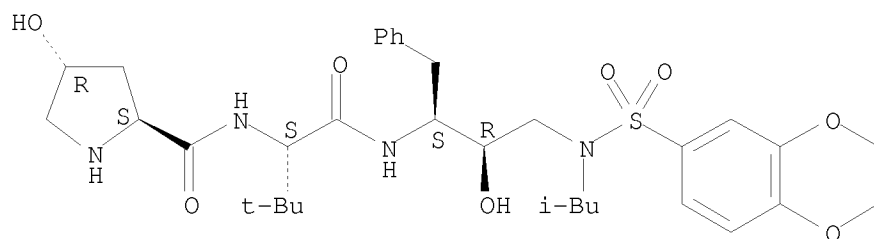


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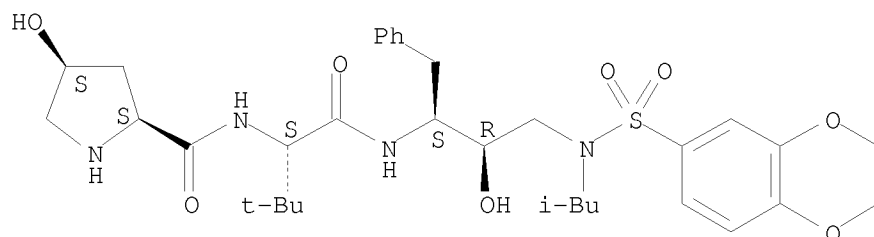
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Absolute stereochemistry.



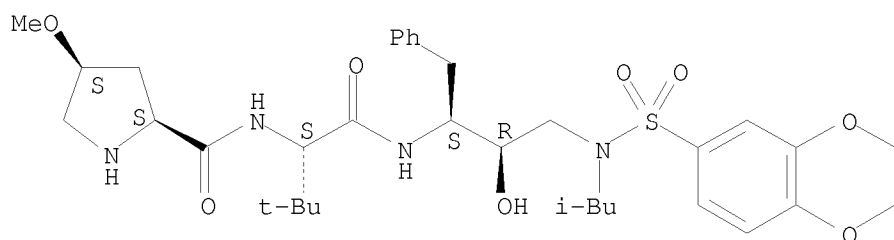
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Absolute stereochemistry.



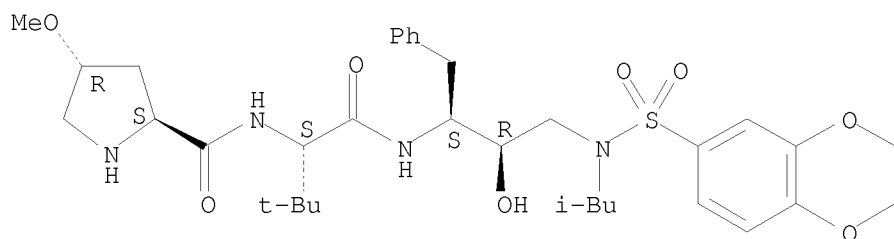
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Absolute stereochemistry.



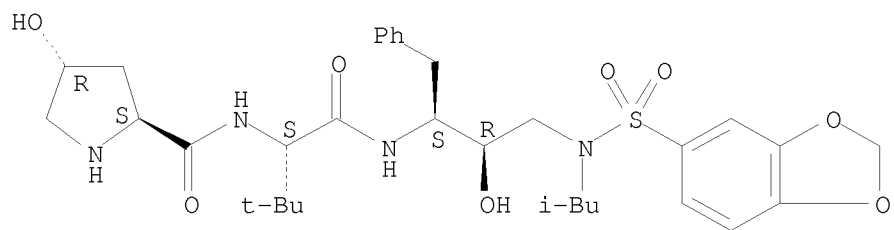
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Absolute stereochemistry.



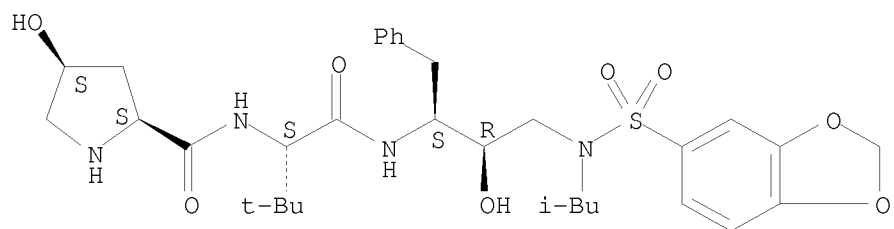
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CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



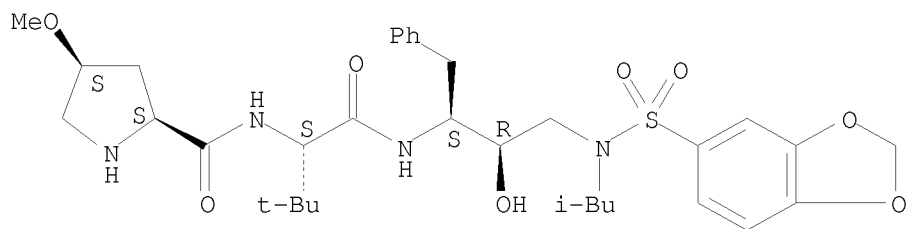
RN 1140058-18-9 CAPLUS  
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



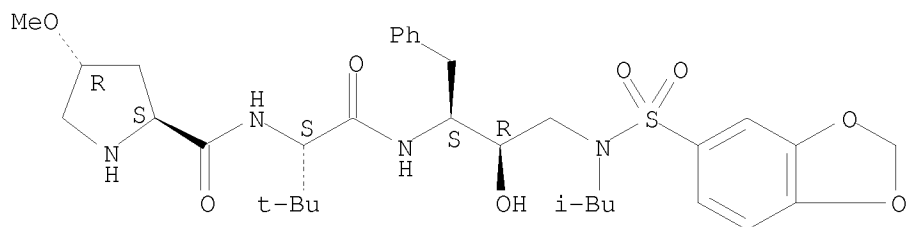
RN 1140058-22-5 CAPLUS  
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



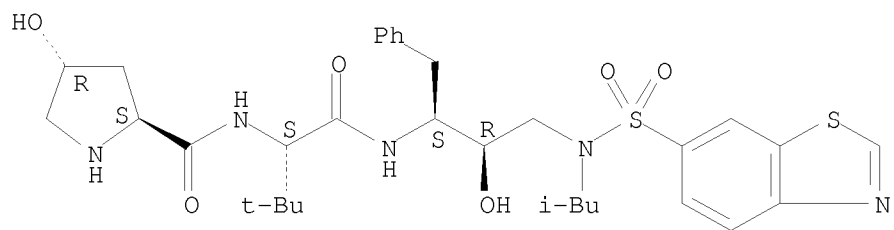
RN 1140058-26-9 CAPLUS  
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



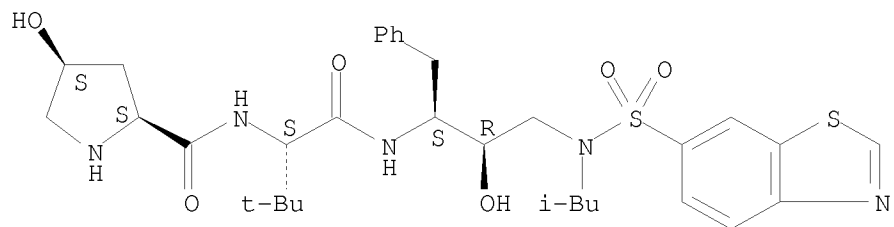
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CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



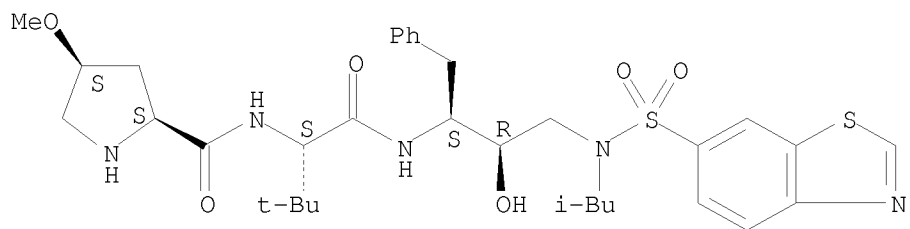
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CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



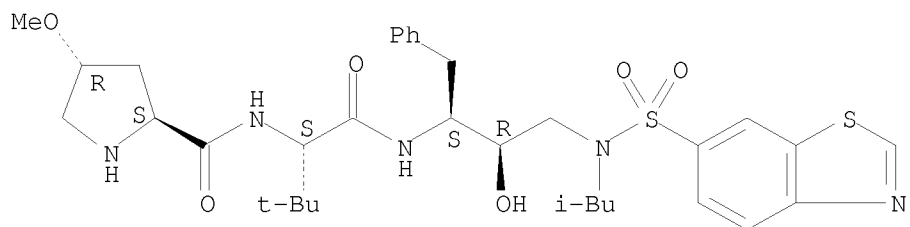
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CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



RN 1140058-41-8 CAPLUS  
CN INDEX NAME NOT YET ASSIGNED

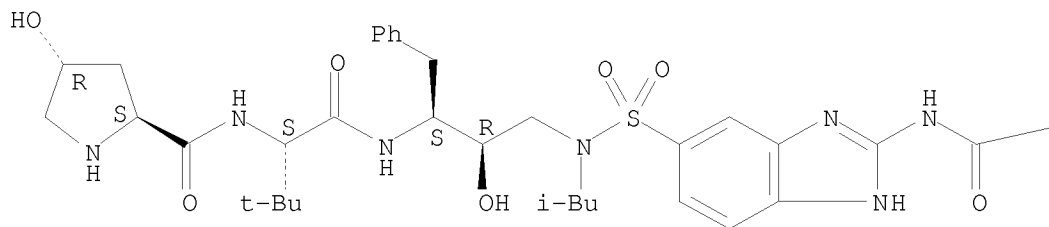
Absolute stereochemistry.



RN 1140058-45-2 CAPLUS  
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

PAGE 1-A



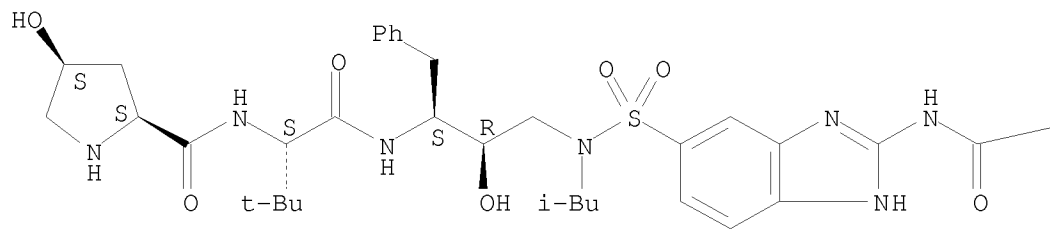
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RN 1140058-48-5 CAPLUS  
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

PAGE 1-A



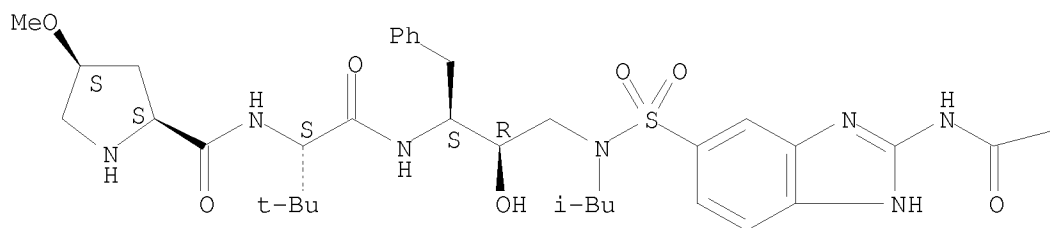
PAGE 1-B

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RN 1140058-52-1 CAPLUS  
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

PAGE 1-A



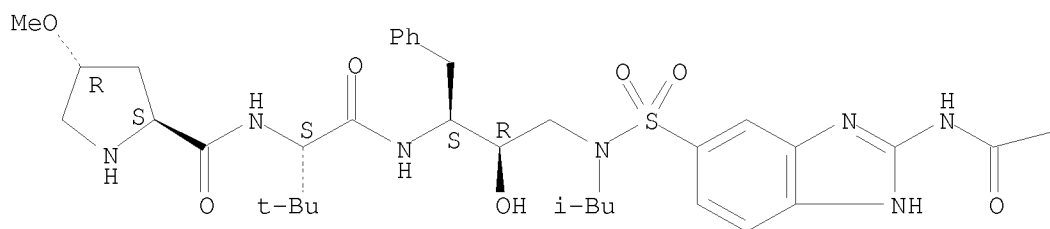
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RN 1140058-56-5 CAPLUS  
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

PAGE 1-A



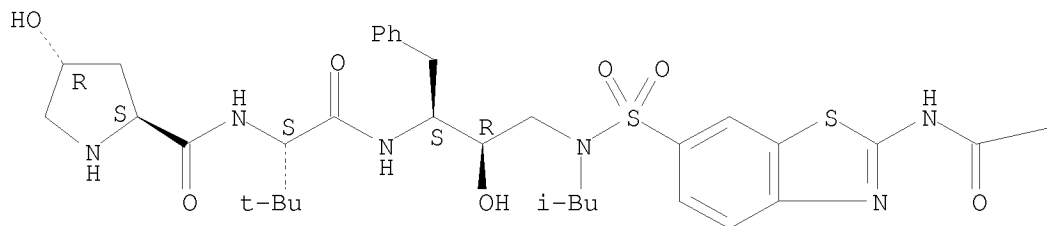
PAGE 1-B

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RN 1140058-60-1 CAPLUS  
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

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REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS  
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FILE 'REGISTRY' ENTERED AT 11:11:46 ON 18 JUN 2009

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L2 6 S L1 SSS SAM

L3 4301 S L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 11:16:22 ON 18 JUN 2009

L4 0 S L3 AND THREOS?

L5 352 S L3

L6 11 S L5 AND HIV

=> s threos?

L7 669 THREOS?

=> s l7 and hiv

85291 HIV

L8 7 L7 AND HIV

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L8 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN  
 ED Entered STN: 28 Nov 2008  
 ACCESSION NUMBER: 2008:1431610 CAPLUS  
 DOCUMENT NUMBER: 150:701  
 TITLE: Computer aided ligand-based and receptor-based drug  
 design utilizing molecular shape and electrostatic  
 complementarity  
 INVENTOR(S): Zauhar, Randy J.; Welsh, William J.  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 51pp., Cont.-in-part of U.S.  
 Ser. No. 635,280, abandoned.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20080294404	A1	20081127	US 2007-870279	20071010
PRIORITY APPLN. INFO.:			US 2002-401637P	P 20020806
			US 2003-635280	B2 20030806

AB Methods related to the generation of shape signatures representing mol.  
 shape, and using shape signatures in both ligand-based and receptor-based  
 mol. design. Ray-tracing is used to explore the volume interior to a  
 ligand, or the space exterior to a receptor site. Shape signatures are  
 then probability distributions derived from the ray-traces. Shape  
 signatures provide condensed descriptors of shape properties readily  
 compared to each other to test for shape similarity or complementarity.

L8 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN  
 ED Entered STN: 08 Aug 2008  
 ACCESSION NUMBER: 2008:953805 CAPLUS  
 TITLE: Probing the interaction of HIV reverse  
 transcriptase with conformationally locked  
 threosyl nucleoside phosphonates: A  
 stereochemical approach  
 AUTHOR(S): Saneyoshi, Hisao; Vu, B. Christie; Hughes, Stephen H.;  
 Boyer, Paul L.; Sarafianos, Stefan G.; Marquez, Victor  
 E.  
 CORPORATE SOURCE: Laboratory of Medicinal Chemistry, Center for Cancer  
 Research, NCI-Frederick, Frederick, MD, 21702, USA  
 SOURCE: Abstracts of Papers, 236th ACS National Meeting,  
 Philadelphia, PA, United States, August 17-21, 2008  
 (2008), MEDI-332. American Chemical Society:  
 Washington, D. C.  
 CODEN: 69KXQ2  
 DOCUMENT TYPE: Conference; Meeting Abstract; (computer optical disk)  
 LANGUAGE: English

AB Nucleoside phosphonates are an important category of antiviral agents,  
 which can bypass the inefficient, and rate-limiting first phosphorylation  
 step. A nucleoside phosphonate can be further phosphorylated by cellular  
 kinases to produce the required triphosphate congener. Recently,  
 Herdewijn et. al. reported that deoxy-L-threosylphosphonate  
 nucleosides are effective anti-HIV agents. This innovative  
 report inspired us to synthesize nucleoside phosphonates of  
 conformationally locked carbocyclic nucleosides to probe their  
 interactions with the active site of HIV-1 RT. We synthesized a  
 conformationally locked, carbocyclic nucleoside phosphonate version of the  
 active L-threosyl analog built on a rigid bicyclo[3.1.0]hexane  
 template from chiral cyclopentene monoacetate. The structure of the

precursor was confirmed by X-ray crystallog. However, the compound was inactive against HIV-1 possibly due to a steric clash with M184. The synthesis of the D-enantiomer, which according to modeling should avoid this clash, is in progress and results with this compound will be presented.

L8 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN

ED Entered STN: 22 Mar 2005

ACCESSION NUMBER: 2005:245689 CAPLUS

DOCUMENT NUMBER: 142:385090

TITLE: Deoxythreosyl phosphonate nucleosides as selective anti-HIV agents

AUTHOR(S): Wu, Tongfei; Froeyen, Matheus; Kempeneers, Veerle; Pannecouque, Christophe; Wang, Jing; Busson, Roger; De Clercq, Erik; Herdewijn, Piet

CORPORATE SOURCE: Laboratories of Medicinal Chemistry and Virology, Rega Institute for Medical Research, Louvain, Belg.

SOURCE: Journal of the American Chemical Society (2005), 127(14), 5056-5065

CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 142:385090

AB Out of a series of eight new phosphonate nucleosides with an L-threose and an L-2-deoxythreose sugar moiety, two new compds. were identified (PMDTA and PMDIT) that showed potent anti-HIV-1 (HIV-2) activity [EC<sub>50</sub> = 2.53  $\mu$ M (PMDTA) and 6.59  $\mu$ M (PMDIT)], while no cytotoxicity was observed at the highest concentration tested

[CC<sub>50</sub> > 316  $\mu$ M (PMDTA) and > 343  $\mu$ M (PMDIT)]. The kinetics of incorporation of PMDTA into DNA (using the diphosphate of PMDTA as substrate and HIV-1 reverse transcriptase as catalyst) was similar to the kinetics observed for dATP, while the diphosphate of PMDTA was a very poor substrate for DNA polymerase  $\alpha$ . The incorporated PMDTA fits very well in the active site pocket of HIV-1 reverse transcriptase.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN

ED Entered STN: 19 Nov 2003

ACCESSION NUMBER: 2003:901969 CAPLUS

DOCUMENT NUMBER: 140:104451

TITLE: Shape Signatures: A New Approach to Computer-Aided Ligand- and Receptor-Based Drug Design

AUTHOR(S): Zauhar, Randy J.; Moyna, Guillermo; Tian, LiFeng; Li, ZhiJian; Welsh, William J.

CORPORATE SOURCE: Department of Chemistry Biochemistry, University of the Sciences in Philadelphia, Philadelphia, PA, 19104, USA

SOURCE: Journal of Medicinal Chemistry (2003), 46(26), 5674-5690

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A unifying principle of rational drug design is the use of either shape similarity or complementarity to identify compds. expected to be active against a given target. Shape similarity is the underlying foundation of ligand-based methods, which seek compds. with structure similar to known

actives, while shape complementarity is the basis of most receptor-based design, where the goal is to identify compds. complementary in shape to a given receptor. These approaches can be extended to include mol. descriptors in addition to shape, such as lipophilicity or electrostatic potential. Here we introduce a new technique, which we call shape signatures, for describing the shape of ligand mols. and of receptor sites. The method uses a technique akin to ray-tracing to explore the volume enclosed by a ligand mol., or the volume exterior to the active site of a protein. Probability distributions are derived from the ray-trace, and can be based solely on the geometry of the reflecting ray, or may include joint dependence on properties, such as the mol. electrostatic potential, computed over the surface. Our shape signatures are just these probability distributions, stored as histograms. They converge rapidly with the length of the ray-trace, are independent of mol. orientation, and can be compared quickly using simple metrics. Shape signatures can be used to test for both shape similarity between compds. and for shape complementarity between compds. and receptors and thus can be applied to problems in both ligand- and receptor-based mol. design. We present results for comparisons between small mols. of biol. interest and the NCI Database using shape signatures under two different metrics. Our results show that the method can reliably extract compds. of shape (and polarity) similar to the query mols. We also present initial results for a receptor-based strategy using shape signatures, with application to the design of new inhibitors predicted to be active against HIV protease.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN

ED Entered STN: 04 Nov 2003

ACCESSION NUMBER: 2003:862516 CAPLUS

DOCUMENT NUMBER: 140:73032

TITLE: Recognition of threosyl nucleotides by DNA and RNA polymerases

AUTHOR(S): Kempeneers, Veerle; Vastmans, Karen; Rozenski, Jef; Herdewijn, Piet

CORPORATE SOURCE: Rega Institute for Medical Research, Laboratory for Medicinal Chemistry, Louvain, B-3000, Belg.

SOURCE: Nucleic Acids Research (2003), 31(21), 6221-6226  
CODEN: NARHAD; ISSN: 0305-1048

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB  $\alpha$ -L- Threose nucleic acids (TNA) are potentially natural nucleic acids that could have acted as an evolutionary alternative to RNA. The authors determined whether DNA or RNA polymerases could recognize phosphorylated threosyl nucleosides. The authors found that for both the Vent (exo-) DNA polymerase and HIV reverse transcriptase, Km values were increased and kcat values decreased for the incorporation of tTTP in comparison to their natural counterparts. The results suggest that TNA may have played a role in the evolution of the DNA-RNA-protein world. Thus, TNA may be a candidate for further studies in evolutionary chemical and biol.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN

ED Entered STN: 15 Jul 2003

ACCESSION NUMBER: 2003:537722 CAPLUS

DOCUMENT NUMBER: 139:225996

TITLE: TNA Synthesis by DNA Polymerases

AUTHOR(S): Chaput, John C.; Szostak, Jack W.  
CORPORATE SOURCE: Department of Molecular Biology, Howard Hughes Medical  
Institute, Boston, MA, 02114, USA  
SOURCE: Journal of the American Chemical Society (2003),  
125(31), 9274-9275  
CODEN: JACSAT; ISSN: 0002-7863  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Threose nucleic acid (TNA), which has a repeat unit one atom  
shorter than that of DNA, is capable of Watson-Crick base pairing with  
DNA, RNA, and TNA. Because of its chemical simplicity, TNA is considered to  
be a possible progenitor of RNA. As an initial step toward developing the  
mol. tools necessary to investigate the functional capabilities of TNA by  
in vitro selection, we have screened a variety of DNA polymerases for TNA  
synthesis activity on a DNA template. We wish to report that several  
polymerases show surprisingly good ability to synthesize TNA using  
 $\alpha$ -L-threofuranosyl thymidine-3'-triphosphate as a substrate.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN

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TITLE: Grignard Addition to Aldonitrones. Stereochemical  
Aspects and Application to the Synthesis of  
C2-Symmetric Diamino Alcohols and Diamino Diols

AUTHOR(S): Dondoni, Alessandro; Perrone, Daniela; Rinaldi,  
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CORPORATE SOURCE: Dipartimento di Chimica Laboratorio di Chimica  
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LANGUAGE: English

OTHER SOURCE(S): CASREACT 130:138879

AB A new example of the stereoselective installation of the amino group at a  
saturated carbon center via organometallic addition of chiral aldehydes to  
nitrones is illustrated by the synthesis of 1,3-diamino-2-propanol,  
RC(NH<sub>2</sub>)CH(OH)CH(NH<sub>2</sub>)R (I), and 1,4-diamino-2,3-butanediol,  
RCH(NH<sub>2</sub>)CH(OH)CH(OH)CH(NH<sub>2</sub>)R (II), units. Three diamino alc. I  
stereotriads were obtained by stereoselective addition of alkylmagnesium  
halides (benzyl, cyclohexylmethyl, and methallyl) to the N-benzyl nitrones  
derived from  $\beta$ -amino- $\alpha$ -hydroxy aldehydes, followed by reduction of  
the resulting N-benzylhydroxylamines. Three 1,4-dibenzyl substituted  
stereoisomers of type II with fixed S configuration at C2 and C3 were  
prepared by sequential and simultaneous amination in two directions starting  
from L-threose nitron and L-tartraldehyde bis-nitron, resp.  
The R,S,S,R isomer obtained by the former route was converted to a  
seven-membered ring cyclic urea (1,3-diazepin-2-one), i.e., a compound that  
belongs to a class of nonpeptide HIV-1 protease inhibitors.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT